JUN 13 1947 ©C18 81323

Vol. 21 MAY, 1947 No. 5

SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

EDITORS

ALTON OCHSNER, New Orleans OWEN H. WANGENSTEEN, Minneapolis

ASSOCIATE EDITOR

ALFRED BLALOCK, Baltimore

Original Communications

Chemosurgical Treatment of Cancer of the Ear: A Microscopically Controlled Method of Excision. Frederic E. Mohs, M.D., Madison, Wis. ---- 605

Successful Suture of the Abdominal Aorta for Arteriovenous Fistula. Lieutenant Colonel Norman E. Freeman and Lieutenant Colonel Ambrose H. Storck, Medical Corps, Army of the United States ---- 623

Evaluation of the Basal Vascular Tone Test as an Indication for Sympathectomy in the Treatment of Surgical Lesions of the Major Arteries. Captain E. W. Rector, Medical Corps, Army of the United States ---- 630

The Fluorescin Wheal Test for Collateral Circulation in the Preoperative Evaluation of Patients With Aneurysms and Arteriovenous Fistulas. Captain Theodore B. Massell, Medical Corps, Army of the United States ---- 636

Direct Measurement of Blood Pressure Within Arterial Aneurysms and Arteriovenous Fistulas. Lieutenant Colonel Norman E. Freeman, Medical Corps, Army of the United States ---- 646

A Method of Rapid Transfusion Into the Femoral Vessels in Patients Without Adequate Peripheral Superficial Veins. J. Ordie Shaffer, M.D., Minneapolis, Minn. ---- 659

Wound Healing Studies on Several Substances Recommended for the Treatment of Burns. Brock E. Brush, M.D., Conrad R. Lam, M.D., and Joseph L. Ponka, M.D., Detroit, Mich. ---- 662

The Treatment of Bedsores in Paraplegic Patients. Major Bromley S. Freeman, Medical Corps, Army of the United States ---- 668

Acute Cholecystitis. L. J. Lester, M.D., New York, N. Y. ---- 675

Intrathecal Penicillin in Bacterial Meningitis. Robert G. Livingstone, M.D., Boston, Mass., and John E. Leach, M.D., New York, N. Y. ---- 683

Intra-arterial Penicillin in the Surgical Treatment of Infections of the Extremities. J. Ordie Shaffer, M.D., Minneapolis, Minn. ---- 692

The Importance of Precise Bacteriologic Data in the Treatment of Infections of the Urogenital Tract. Joseph A. Lazarus, M.D., and Lewis H. Schwarz, B.S., New York, N. Y. ---- 713

The Postgastrectomy Syndrome. David Adlersberg, M.D., and Ernst Hammerschlag, M.D., New York, N. Y. ---- 720

Three Hundred Seventy-Four Acute War Wounds of the Thorax. Charles B. Burbank, M.D., Boston, Mass., William H. Falor, M.D., Akron, Ohio, and Howard W. Jones, Jr., M.D., Baltimore, Md. ---- 730

(Continued on inside back cover)

Published by THE C. V. MOSBY COMPANY, St. Louis, U. S. A.

Copyright 1947 By The C. V. Mosby Company

SURGERY

ADVISORY COUNCIL

DONALD C. BALFOUR, Rochester, Minn.
VILRAY P. BLAIR, St. Louis
BARNEY BROOKS, Nashville
ELLIOTT C. CUTLER, Boston
WILLIAM E. GALLIE, Toronto
EVARTS A. GRAHAM, St. Louis
HOWARD C. NAFFZIGER, San Francisco
HARVEY B. STONE, Baltimore
ALLEN O. WHIPPLE, New York City

EDITORIAL BOARD

FREDERICK A. COLLER, Ann Arbor
EDWARD D. CHURCHILL, Boston
VERNON C. DAVID, Chicago
LESTER R. DRAGSTEDT, Chicago
RALPH K. GHORMLEY, Rochester, Minn.
ROSCOE R. GRAHAM, Toronto
SAMUEL C. HARVEY, New Haven
FRANK HINMAN, San Francisco
EMILE F. HOLMAN, San Francisco
EDWIN P. LEHMAN, University, Va.
FRANK L. MELENEY, New York City
JOHN J. MORTON, Rochester, N. Y.
THOMAS G. ORR, Kansas City, Kan.
GEORGE T. PACK, New York, N. Y.
WILDER G. PENFIELD, Montreal
ISIDOR S. RAVDIN, Philadelphia
WILLIAM F. RIENHOFF, JR., Baltimore

COMMITTEE ON PUBLICATIONS

ARTHUR W. ALLEN
Boston, Mass.

CLAUDE S. BECK
Cleveland, Ohio.

ELEXIOUS T. BELL
Minneapolis, Minn.

ISAAC A. BIGGER
Richmond, Va.

ALBERT C. BRODERS
Rochester, Minn.

J. BARRETT BROWN
St. Louis, Mo.

ALEXANDER BRUNSCHWIG
Chicago, Ill.

LOUIS A. BUIE
Rochester, Minn.

WARREN H. COLE
Chicago, Ill.

C. D. CREEVY
Minneapolis, Minn.

GEORGE M. CURTIS
Columbus, Ohio

M. DE BAKEY
New Orleans, La.

WILLIAM J. DIECKMANN
Chicago, Ill.

DANIEL C. ELKIN
Atlanta, Ga.

WILLIS D. GATCH
Indianapolis, Ind.

CHARLES F. GESCHICKTER
Baltimore, Md.

J. MASON HUNDLEY, JR.
Baltimore, Md.

ANDREW C. IVY
Chicago, Ill.

DENNIS E. JACKSON
Cincinnati, Ohio

J. ALBERT KEY
St. Louis, Mo.

CHAUNCEY LEAKE
Galveston, Texas

FRANCIS E. LEJEUNE
New Orleans, La.

HAROLD I. LILLIE
Rochester, Minn.

JOHN S. LUNDY
Rochester, Minn.

FRANK C. MANN
Rochester, Minn.

CHARLES W. MAYO
Rochester, Minn.

ROBERT L. PAYNE
Norfolk, Va.

LEO G. RIGLER
Minneapolis, Minn.

ERNEST SACHS
St. Louis, Mo.

ARTHUR M. SHIPLEY
Baltimore, Md.

ALBERT O. SINGLETON
Galveston, Texas

MAURICE B. VISSCHER
Minneapolis, Minn.

RALPH M. WATERS
Madison, Wis.

JAMES C. WHITE
Boston, Mass.

PHILIP D. WILSON
New York, N. Y.

JOHN A. WOLFER
Chicago, Ill.

Vol. 21, No. 5, May, 1947. Surgery is published monthly by The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. Subscription price: United States, its possessions, Pan-American Countries, $10.00 a year; Canada and Foreign, $11.00. Entered as Second-Class Matter January 20, 1937, at the Post Office at St. Louis, Missouri, under the Act of March 3, 1879. Printed in U. S. A.

New Instruments for Fine Surgery

in the relief of HYPERTENSION

THE authoritative design of every Pilling instrument is the natural result of continuous, close cooperation with acknowledged leaders in surgery throughout the world.

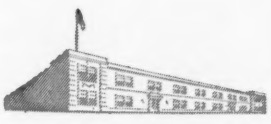
The group of instruments illustrated here was designed by R. H. Smithwick, M.D. for use in his recently introduced two-stage lumbo-dorsal splanchnicectomy for the relief of hypertension.* The Willauer Scissors, shown at the right, are also used by Dr. Smithwick in this operative procedure.

These and many other new instruments of special and authentic design are now available to the surgical profession. Write today for detailed information to George P. Pilling & Son Company, 3451 Walnut Street, Philadelphia 4, Pa.

**Cleveland Clinic Quarterly, 12:105-117, Oct., 1945*

1. **P15532** Smithwick Hook and Spatula
2. **P15530** Smithwick Hook
3. **P15522** Smithwick Clip-Applying Forceps
4. **P15524** Smithwick Clip Rack
   P15526 Cut Clips (not illustrated)
5. **P15534** Hartmann Type Forceps, large
   P16765 Willauer Scissors, straight, 17 cm.
6. **P16766** Same, curved, 17 cm.
   P16767 Same, straight, 25 cm.
   P16768 Same, curved, 25 cm.
   P16769 Same, straight, 30 cm.
   P16770 Same, curved, 30 cm.

INSTRUMENTS BY— Pilling



Instrument Craftsmen Since 1814

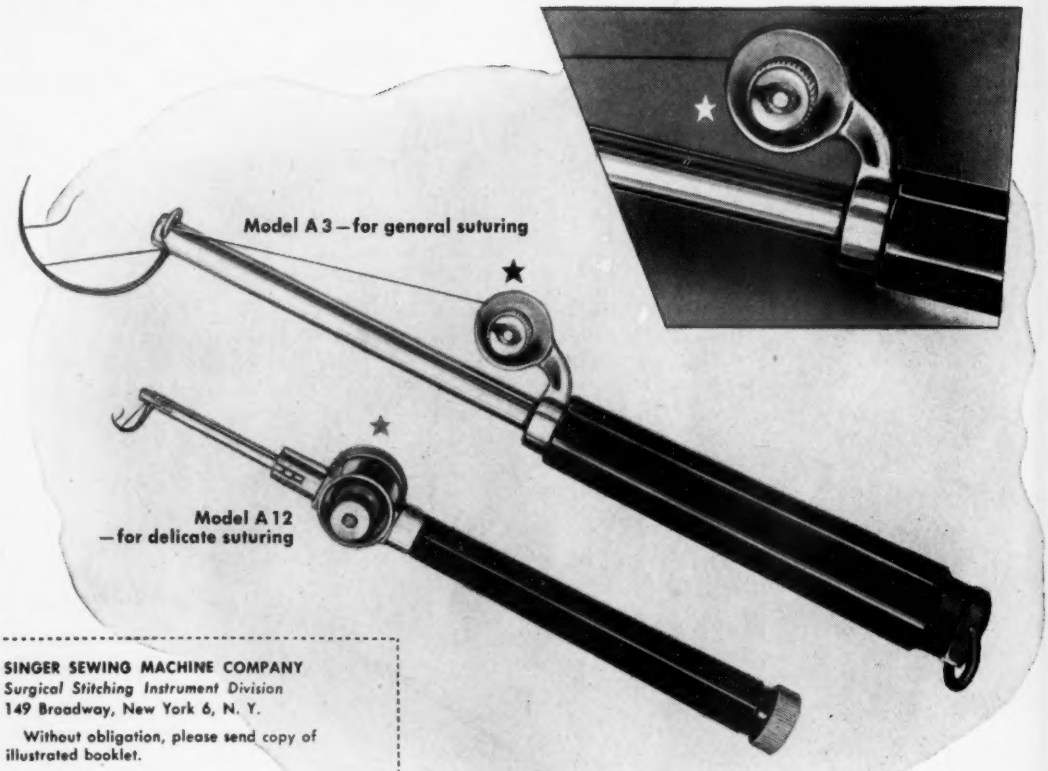
Better Surgery

THROUGH CLOSER CONTROL OF SUTURE MATERIAL

The increasing number of surgeons who are using the new Singer Surgical Stitching Instruments find particularly valuable the closer control of suturing material which these instruments afford. • The unique construction allows continuous feeding of any standard suturing material from the spool, by light pressure on the nut directly under constant thumb control—with no long, loose ends to break asepsis by contacting contaminated fields. This continuous feeding provides unprecedented suturing capacity, and shortens the time required for the suturing phase of operative procedures. • These advantages derive from the functional incorporation of needle, holder, suture supply, and (with some needles) a cutting edge—all in one single instrument. There are many other remarkable features inherent in the Singer instruments. May we forward a comprehensively illustrated booklet with full details?

SINGER

SURGICAL STITCHING INSTRUMENT



SINGER SEWING MACHINE COMPANY
Surgical Stitching Instrument Division
149 Broadway, New York 6, N. Y.

Without obligation, please send copy of illustrated booklet.

Name_____

Address_____

City_____ State_____

B-57

Our two newest films available for showing are (1) "Rehabilitation of Parkinson's Syndrome," and (2) "Treatment of Major Neuralgias."

COPYRIGHT, U.S.A., 1946, BY THE SINGER MANUFACTURING CO. ALL RIGHTS RESERVED FOR ALL COUNTRIES.

D&G CLAUSTRO-THERMAL BOILABLE CATGUT

Surgeons who prefer a boilable suture can rely on D&G Claustro-Thermal* Catgut for a controlled balance of characteristics necessary to meet every surgical situation. Obtainable with swaged-on Atraumatic needles developed in collaboration with eminent surgical authorities . . . Claustro-Thermal Catgut Sutures are the product of D&G research, an assurance of the ultimate in suture quality. Obtainable through responsible dealers everywhere. Davis & Geck, Inc., Brooklyn, New York.

D&G Sutures

"This One Thing We Do"

Reg. U. S. Pat. Off.

when it's a question of— DERMAL SUTURES

What special treatment must be given dermal sutures in order to make them soft and pliable?

No special treatment is necessary if Champion DERMAL Sutures are used. A new, exclusive GUDEBROD manufacturing refinement makes it possible to produce this dermal suture soft and pliable, easy to handle, ready for immediate use without previous preparation. A special finish makes it impossible for the Champion DERMAL Suture to crack or fray in use; knots will not slip; and neither skin nor tissue will adhere to the strand.

the answer is GUDEBROD

Manufacturers of CHAMPION sutures, preferred by leading surgeons for more than 75 years.

GUDEBROD BROTHERS SILK CO., INC.
225 West 34th Street, New York 1, N. Y.
PHILADELPHIA · BOSTON · LOS ANGELES

GUDEBROD BROS. CHAMPION

Champion Paré SERUM-PROOF SILK • Champion SURGEON'S SILK (untreated) • Champion DERMAL-TENSION SUTURES • Champion SILK STERILE TUBE SUTURES • Champion SERUM-PROOF NYLON SUTURES • Hand Craft COTTON SUTURES • Champion LINEN SUTURES • Champion UMBILICAL TAPE

May we send you a 40 inch trial suture?

When cycles cease at the menopause, Di-Ovocylin relieves the psychosomatic distress that usually follows. A single injection will control symptoms for from 7 to 14 days—far longer than other estrogenic preparations.

CIBA

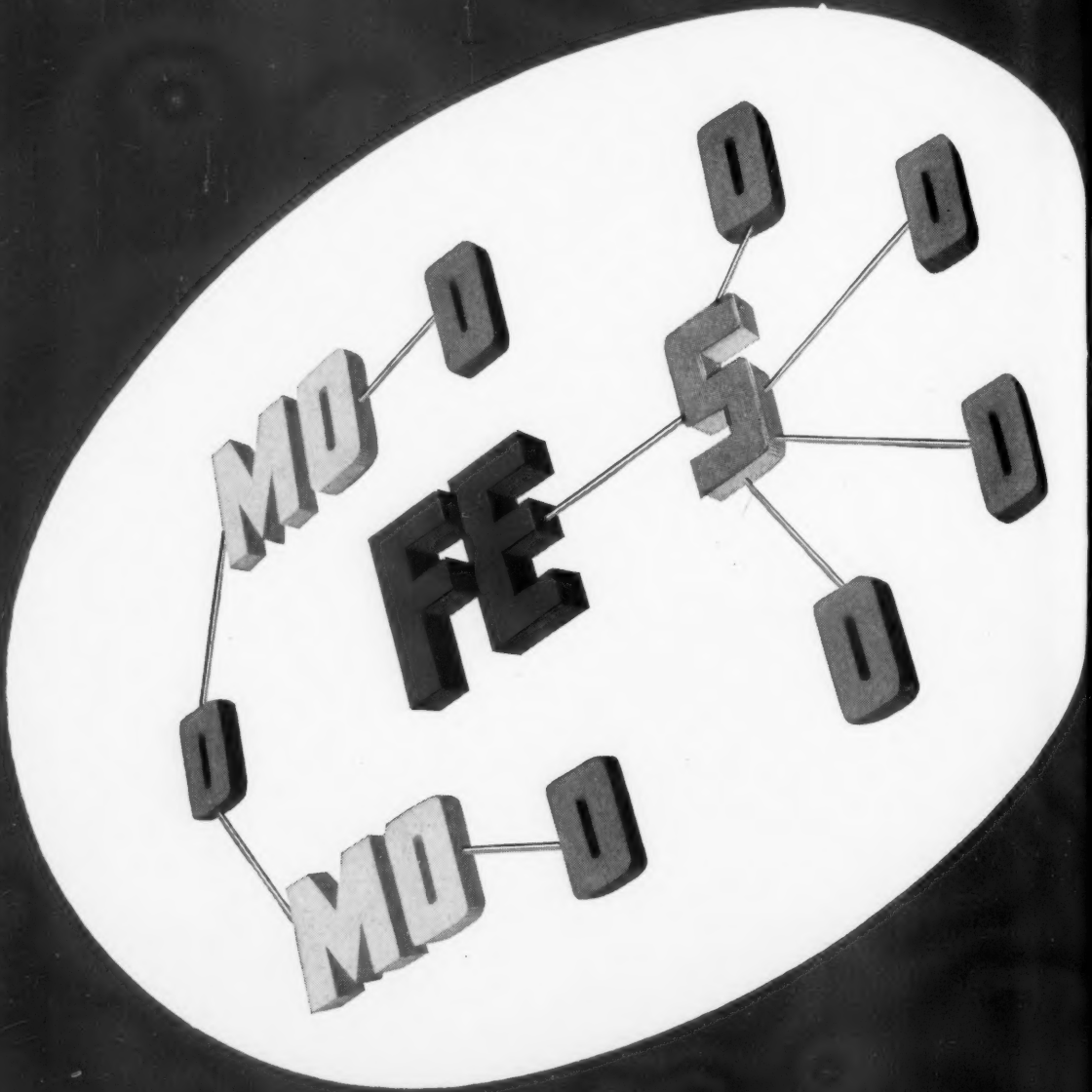
Di-Ovocylin

DI-OVOCYLIN (brand of α-estradiol dipropionate). T. M. Reg. U. S. Pat. Off. and Canada.

For further information, write Professional Service Department.

CIBA PHARMACEUTICAL PRODUCTS, INC. SUMMIT, NEW JERSEY

demonstrably superior



White

White's

LABORATORIES, INC. Pharmaceutical Manufacturers, Newark 7, N. J.

iron utilization in hypochromic anemias

Controlled clinical studies conducted on patients with hypochromic anemia reveal the therapeutic superiority of molybdenized ferrous sulfate over equivalent dosages of ferrous sulfate alone:

MORE RAPID RECOVERY—Normal hemoglobin values are restored more rapidly, increases in the rate of hemoglobin formation being as great as 100% or more in patients studied.

INCREASED UTILIZATION—Iron utilization is similarly more complete.

BETTER TOLERANCE—Gastrointestinal tolerance is excellent—even among patients who have previously shown marked gastrointestinal reactions following oral administration of other iron preparations.*

White's Mol-Iron is a specially processed, co-precipitated complex of molybdenum oxide 3 mg. (1/20 gr.) and ferrous sulfate 195 mg. (3 gr.). Bottles of 100 and 1000 tablets.

*Healy, J. C.: Hypochromic Anemia: Treatment with Molybdenum-Iron Complex, The Journal-Lancet, *66*:218-221 (July) 1946.

Mol-iron *Tablets*

(Molybdenized ferrous sulfate)

GRATEFUL COMFORT
and a quicker recovery
AFTER ANORECTAL SURGERY
with

Bland diet
Analgesia
Sedation
and ... **Petrogalar** *

First postoperative day—1 *tablespoonful* 3 times daily
Thereafter—1 *teaspoonful* 3 times daily

*Am. J. Surg. 72:16, 1946

Petrogalar

Reg. U. S. Pat. Off.

An aqueous suspension of mineral oil, 65%. In pint bottles.

It mixes with the feces to produce a soft, formed, yielding and easily passed stool.

WYETH Incorporated • Philadelphia 3, Pa.

Wyeth®

® Trade Mark Reg. U.S. Pat. Off.

DIAGNOSIS BY TRIAL

Unlike the menopause, the male climacteric is neither heralded by any dramatic change in organ physiology nor detectable by any simple laboratory procedure. The ORETON diagnostic test for androgen deficiency in middle-aged men is, therefore, a singular contribution to endocrine diagnosis and therapy. It proves the existence of the male climacteric when present and restores the patient to a state of well-being. ORETON (testosterone propionate) 25 mg. injected daily five days per week for two weeks will cause a disappearance of symptoms etiologically related to failing testicular function.

ORETON

For maintenance therapy of the male climacteric, ORETON should be injected in doses of 25 mg. two to three times weekly, gradually reducing the dosage to ascertain the individual demand. ORETON-M (methyltestosterone) Tablets of 10 mg. may be substituted to maintain hormonal balance.

ORETON, testosterone propionate in oil, ampules of 1 cc. containing 5, 10 and 25 mg.; boxes of 3, 6 and 50 ampules. Also in 10 cc. multiple dose vials containing 25 and 50 mg. per cc. ORETON-M Tablets of 10 mg. methyltestosterone; boxes of 15, 40 and 100 tablets.

Trade-Marks ORETON and ORETON-M—Reg. U. S. Pat. Off.

SCHERING

Schering CORPORATION · BLOOMFIELD, N. J.

IN CANADA, SCHERING CORPORATION LIMITED, MONTREAL

You Should Subscribe Now for These Special Journals

American Journal of Obstetrics and Gynecology

Representing The American Gynecological Society, The American Association of Obstetricians, Gynecologists and Abdominal Surgeons, and nine other societies. Editors: Geo. W. Kosmak, M.D.; Associate Editors: Howard C. Taylor, Jr., M.D., and Wm. J. Dieckmann, M.D.

Published monthly. Subscription rates: Domestic and for the Pan-American Countries, $10.00; Canada, and other Foreign Countries, $11.00 a year.

The Journal of Pediatrics

Official organ for The American Academy of Pediatrics. Editors: Borden S. Veeder, M.D., and Hugh McCulloch, M.D.

Published monthly. Subscription rates: Domestic and for the Pan-American Countries, $8.50; Canada, and other Foreign Countries, $9.50 a year.

The Journal of Laboratory and Clinical Medicine

Official Publication of the Central Society for Clinical Research, Carl V. Moore, M.D., Editor. Board of Editors: Edgar V. Allen, M.D.; M. A. Blankenhorn, M.D.; George E. Burch, Jr., M.D.; Paul R. Cannon, M.D.; Jerome E. Conn, M.D.; Charles A. Doan, M.D.; Edgar S. Gordon, M.D.; Irvine H. Page, M.D.; Armand J. Quick, M.D.; Wesley W. Spink, M.D.; Cecil J. Watson, Ph.D., M.D.; Arnold D. Welch, Ph.D.; W. Barry Wood, Jr., M.D.

Published monthly. Subscription rates: Domestic and for the Pan-American Countries, $8.50; Canada, and other Foreign Countries, $9.50 a year.

American Journal of Syphilis, Gonorrhea and Venereal Diseases

J. E. Moore, M.D., Editor, Frank W. Reynolds, M.D., Associate Editor. Advisory Editorial Board: A. M. Chesney, M.D.; C. W. Clarke, M.D.; R. D. Herrold, M.D.; E. L. Keyes, M.D.; P. A. O'Leary, M.D.; T. Parran, M.D.; P. S. Pelouze, M.D.; J. H. Stokes, M.D.; R. A. Vonderlehr, M.D.

Published bimonthly. Subscription rates: Domestic and for the Pan-American Countries, $7.50; Canada, and other Foreign Countries, $8.00 a year.

The Journal of Thoracic Surgery

Representing The American Association for Thoracic Surgery. E. A. Graham, M.D., Editor; Brian Blades, M.D., and Richard H. Mead, Jr., M.D., Associate Editors.

Advisory Editorial Board: John Alexander, M.D.; Edward Wm. Archibald, M.D.; Edward D. Churchill, M.D.; Leo Eloesser, M.D.; Stuart W. Harrington, M.D.; Howard Lilienthal, M.D.; Rudolph Matas, M.D.

Published bimonthly. Subscription rates: Domestic and for the Pan-American Countries, $7.50; Canada, and other Foreign Countries, $8.00 a year.

American Heart Journal

A Journal for the study of circulation. Published monthly under the editorial direction of The American Heart Association. Editor-in-Chief, Thomas M. McMillan, M.D.; Associate Editors: Wallace M. Yater, M.D., Samuel Bellet, M.D., Louis Laplace, M.D.

Subscription rates: Domestic and for the Pan-American Countries, $10.00; Canada, and other Foreign Countries, $11.00 a year.

The Journal of Allergy

Official Organ of The American Academy of Allergy. H. L. Alexander, M.D., Editor. Editorial Board: M. M. Albert, M.D., J. H. Black; M.D.; M. B. Cohen, M.D.; R. A. Cooke, M.D.; S. M. Feinberg, M.D.; S. B. Hooker, M.D.; F. C. Lowell, M.D.; F. M. Rackemann, M.D.; W. B. Sherman, M.D.; F. A. Simon, M.D.; M. B. Sulzberger, M.D.; L. Tuft, M.D.; M. Walzer, M.D.

Subscription rates: Domestic and for the Pan-American Countries, $7.50; Canada, and other Foreign Countries, $8.00 a year.

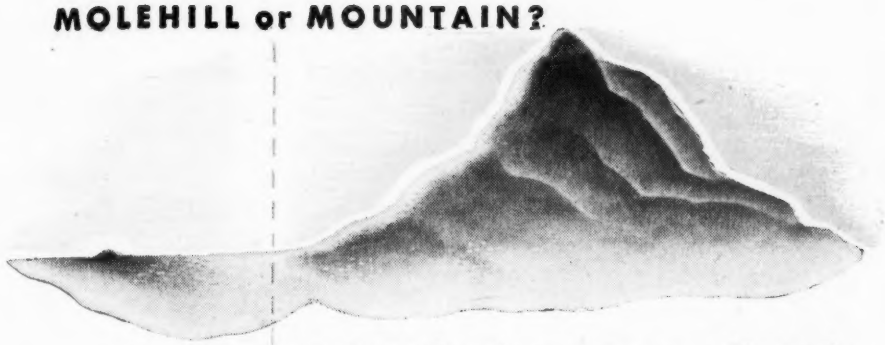
Surgery

Alton Ochsner, M.D., and Owen H. Wangensteen, M.D., Editors. Alfred Blalock, M.D., Associate Editor. Published monthly. Subscription rates: Domestic, $10; Canada, and other Foreign Countries, $11 a year.

☞ Enter your subscriptions to these important special journals today. If you prefer we shall be glad to send a sample copy.

THE C. V. MOSBY COMPANY — *Publishers* — St. Louis

MOLEHILL or MOUNTAIN?



In Constipation—True or Alleged It's MUCILOSE

When the patient who declares himself constipated has made a mountainous problem of over-purgation from a molehill of underlying cause, Mucilose—bland, lubricating bulk—is a valuable adjunct in correcting both the self-imposed laxative habit and the primary intestinal dysfunction.

Ample intestinal bulk is assured by placing the patient on Mucilose—pure, concentrated hemicellulose from psyllium. More efficient... Mucilose absorbs *50 times* its weight of water to form a bland colloidal gel—lubricates the intestinal contents and gently stimulates peristalsis.

For physiologic re-education . . . for more nearly normal evacuation and a regular "habit-time"—*it's Mucilose.*

GREATER BULK from SMALLER DOSE at LOWER COST

Mucilose

IN SPASTIC AND ATONIC CONSTIPATION

Highly purified hemicellulose concentrate, derived from *Plantago loeflingii* . . . available as flakes or granules in 4 oz. bottles and 16 oz. containers.

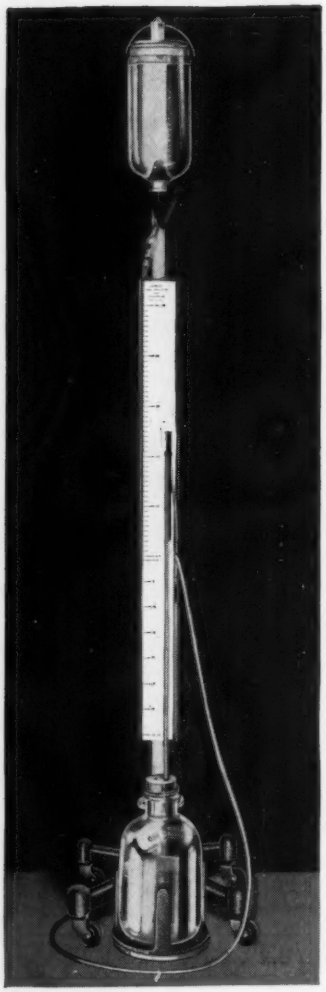
A trial supply of Mucilose will be sent to you upon request.

Frederick Stearns & Company
Division
DETROIT 31, MICHIGAN

NEW YORK • KANSAS CITY • SAN FRANCISCO • ATLANTA • WINDSOR, ONTARIO
SYDNEY, AUSTRALIA • AUCKLAND, NEW ZEALAND

, Trade-Mark Mucilose Reg. U. S. Pat. Off.

Harnessing The Tides!



PATENT PENDING

Tidal Irrigation by

GOMCO

IS REDUCED TO AN EXACT PROCEDURE

SIMPLE! THE DOCTOR simply sets the GOMCO Tidal Irrigator at patient's symphysis pubis level—determines the bladder emptying pressure—and sets the rate of flow of irrigating fluid.

THE NURSE fills the reservoir and empties the receptacle.

DEPENDABLE! The GOMCO Tidal Irrigator does the rest! The procedure is as simple and exact as that... and as trustworthy and efficient as it is simple.

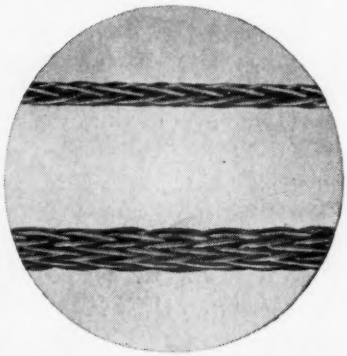
EASY TO KEEP CLEAN, TOO!
Take advantage of this easier, more exact technic. Ask your dealer about the GOMCO Tidal Irrigator, or write:

GOMCO SURGICAL MANUFACTURING CORP.
832M E. FERRY STREET BUFFALO 11, N. Y.

GOMCO EQUIPMENT
Fostering Improved Technics

BRAIDED TANTALUM

A USEFUL, NEW SUTURE MATERIAL



Many individual strands of wire are in Ethicon Braided Tantalum. Photomicrograph, above, shows Sizes 3-0 and 1, magnified to x15.

ETHICON TANTALUM FOR SURGICAL USE

Sutures. Monofilament: Sizes 6-0, 5-0, 4-0. Swaged to Eyeless Atraloc needles. *Braided:* As described at right.

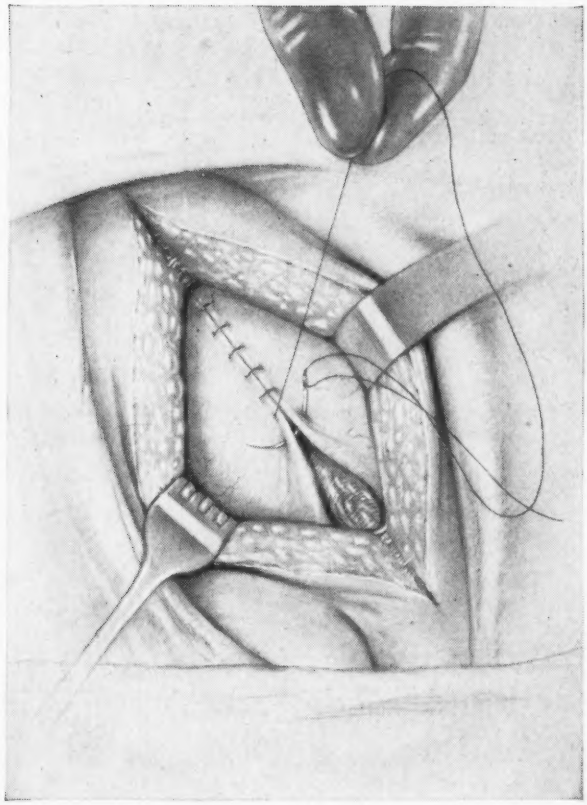
Wire. Suturing material on spools. Sizes 6-0, 5-0, 4-0, 000, 0, 2, 4.

Ribbon. For making neurosurgical hemostasis clips. Clips also supplied ready-made.

Sheet. For skull plates in cranioplasty and general plastic surgery.

Foil. Used in neuro- and orthopedic surgery for protection of nerves and tendons.

Literature describing use of Ethicon Tantalum products available on request.



• Braided tantalum is a new Ethicon suture material which offers the surgeon certain qualities not found in other sutures.

1. Its "handling properties" are superior to monofilament wire. It is much stronger than silk and less variable in size.
2. Its tensile strength is not affected in the presence of infection.
3. When Braided Tantalum is used as a buried suture, the attachment of the tissues to the suture aids greater anchorage.

Ethicon Braided Tantalum Sutures are supplied in Sizes 5-0 to 1, in 60 inch length on card reels.

Braided Tantalum has been found of special value for general surgical closure, plastic surgery, the Guyton operation for ptosis of eyelid and herniorrhaphy.

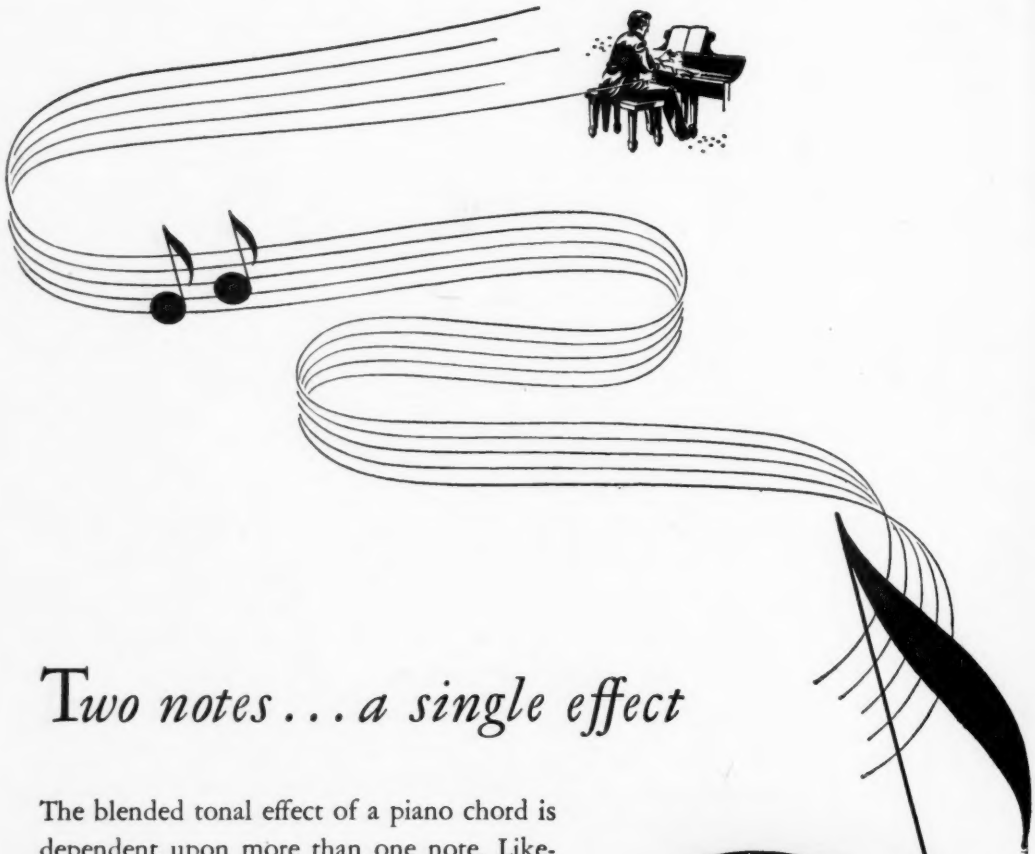
ETHICON

Sutures

FOR EVERY SURGICAL PURPOSE

ETHICON SUTURE LABORATORIES

Division of Johnson & Johnson, New Brunswick, N. J.



Two notes . . . a single effect

The blended tonal effect of a piano chord is dependent upon more than one note. Likewise, a combination of barbiturates can produce a result which cannot be duplicated by a single orally administered barbiturate. With Pulvules Tuinal, a rapid yet prolonged sedative or hypnotic action can be produced. To accomplish this, *rapid* short-acting 'Seconal Sodium' (Sodium Propyl-methyl-carbinyl Allyl Barbiturate, Lilly) is combined with slower *longer*-acting 'Sodium Amytal' (Sodium Isoamyl Ethyl Barbiturate, Lilly). Pulvules Tuinal act promptly and allow the patient a full night's rest, undisturbed by an early awakening.

Available as:
PULVULES TUINAL, 1½ grains (0.1 Gm.)
(No. 303)
and
PULVULES TUINAL, 3 grains (0.2 Gm.)
(No. 304)

Pulvules Tuinal

PULVULES TUINAL—A Combination of 'Seconal Sodium' and 'Sodium Amytal' in Equal Parts

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U. S. A.

SURGERY

VOL. 21 MAY, 1947 NO. 5

Original Communications

CHEMOSURGICAL TREATMENT OF CANCER OF THE EAR: A MICROSCOPICALLY CONTROLLED METHOD OF EXCISION

FREDERIC E. MOHS, M.D., MADISON, WIS.

(From the Department of Surgery and the McArdle Memorial Laboratory, University of Wisconsin Medical School)

THE development of the chemosurgical method for the microscopically controlled excision of cancer has previously been described.[1, 2] The use and evaluation of the method in the treatment of cancer in specific sites, such as the lip[3] and the nose,[4] has been reported. The present article deals with the chemosurgical treatment of cancer of the ear and includes the analysis of the therapeutic results in a consecutive series of 107 lesions treated over the period of nine and one-quarter years ending Sept. 29, 1945, which date is nine months prior to this writing. Inasmuch as the behavior of squamous-cell carcinoma is much different from that of basal-cell carcinoma, the two histologic types are considered separately except in regard to the chemosurgical technique which is the same for both types.

TECHNIQUE

The chemosurgical technique by which cancer of the ear may be excised under systematic microscopic control will be described in the case report which follows.

CASE REPORT.—The lesion pictured in Fig. 1 was first noticed six months previous to the patient's first visit to the Chemosurgery Clinic. It began as a nodule which was covered with skin at first but which became ulcerated after a few weeks. He was referred to a radiologist who in turn referred the patient for chemosurgical treatment because he believed that the cartilage might be damaged by radiation therapy.

The lesion was a firm nodule 11 mm. in diameter. It was elevated 3 mm. above the level of the concha of the ear. There was a central ulcer, in the base of which protruded papillae with slightly hyperkeratotic tips. The lesion was adherent to the underlying cartilage. No enlargement of the regional lymph nodes was palpated.

The first step in treatment was the application of dichloracetic acid to the part of the lesion covered by skin. This keratolytic chemical served to render the skin permeable

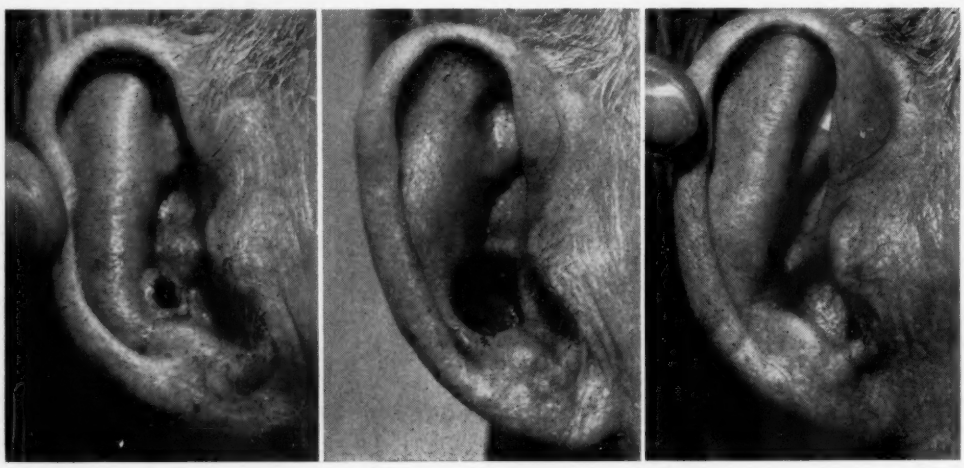
Aided by the Thomas E. Brittingham Fund, the Wisconsin Alumni Research Foundation, and the Jonathan Bowman Memorial Fund.

Received for publication, July 2, 1946.

to the fixative which was next applied. The fixative consists of a paste made up according to the following formula: 40 Gm. of stibnite (80 mesh sieve), 10 Gm. of powdered sanguinaria, and 34.5 c.c. of a saturated solution of zinc chloride. This material was applied in a thickness of about 0.5 millimeter.

The treated area was covered by a layer of cotton and then by an overlapping layer of cotton on which petrolatum was spread to form a moisture-tight closure. The dressing was made fast by means of adhesive tape. The patient was instructed to take 0.65 Gm. of acetylsalicylic acid as required to control the pain. He was treated as an outpatient.

On the second day a layer of tissue about 3 mm. thick was excised with a scalpel. There was no pain or bleeding produced by this operation because the incisions were made through killed and fixed tissue. That cancer was present at this level was evident to gross inspection, so the fixative paste was immediately reapplied in a depth of about 0.2 millimeter. A frozen section of the fixed tissue contained squamous-cell carcinoma of grade 2 malignancy.



A. *B.* *C.*

Fig. 1.—*A*, Squamous-cell carcinoma, grade 2 malignancy, of Group *B* (average diameter, 1 to 2 cm.), located in the concha. *B*, Granulation tissue after separation of the final layer of fixed tissue, including a layer of cartilage, and after healing was under way. *C*, Healed lesion, two months later. Patient is free of cancer after three and one-half years.

On the third day the cancer tissue was still grossly visible and was seen to involve the perichondrium under the central part of the neoplasm. There was, however, no visible erosion of the cartilage itself. Accordingly, the fixative paste was not applied to the cartilage but only to the tissues at the periphery.

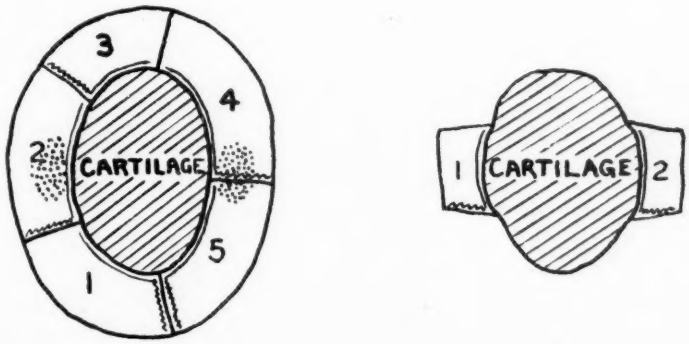
On the fourth day a layer of tissue 1 mm. in thickness was excised from the periphery. Since no cancer could be detected by gross examination the excised layer was divided into five specimens of convenient size, and their locations were mapped on the lesion (using mercurochrome) and on a pad of paper (Fig. 2, *A*).

Frozen sections were made by cutting through the undersurface of each of the flat specimens and by staining with hematoxylin and eosin. Each section was scanned under the microscope and the areas of remaining cancer located on the map as indicated by the two stippled areas in Fig. 2, *A*.

Further application of the fixative was limited to the two cancerous areas. On the next day the specimens from these areas were found to be free of cancer (Fig. 2, *B*). The lesion was covered with a petrolatum gauze dressing.

One week later the remaining thin layer of fixed tissue had become separated from the living tissues and could be removed by snipping the holding strands of fibrous tissue with sharp-pointed scissors. The necrotic portions of cartilage were also removed. (In

this series the average time at which the basal layer could be removed was 7.4 days with a range of from 4 to 12 days.) The granulations (Fig. 1, *B*) were kept covered with petrolatum gauze until the wound had healed two weeks later. The final scar and defect were barely noticeable (Fig. 1, *C*).



A. *B.*

Fig. 2.—Maps showing locations of specimens removed on two successive days from the lesion shown in Fig. 1. *A*, Stippled areas represent two areas of cancer. On the following day specimens from these two areas were free of cancer (*B*).

As in this case, many cancers of the ear extend onto the underlying cartilage. When this occurs it is necessary to section only the tissues at the periphery. If, however, the cancer has eroded through the cartilage, the defect is grossly visible upon exposure of the cartilage and microscopic study of the tissues beyond the invaded cartilage is indicated.

When invasion of the entire thickness of the ear has occurred it is necessary to remove the full thickness of the ear in the involved region (Fig. 3). Cancers which extend far beyond the ear proper are not infrequently encountered (Fig. 4). Some were followed out for many centimeters beyond the region in which the cancer was originally thought to be confined.

The extension of cancer onto the bone necessitates the destruction of a thin layer of bone to assure complete removal of the neoplasm. Cancerous erosion of the bone produces a honeycombed area which is grossly visible; this involved bone may be fixed with the zinc chloride fixative and removed layer by layer with chisels or rongeurs, until solid, cancer-free bone is reached.

Removal of large lesions involving the helix of the ear may necessarily result in the formation of a niche in the normal contour of the ear. Such defects are relatively easy to repair, however, because a maximum amount of normal structure is preserved as a base for plastic reconstruction.

In cases in which the entire ear was removed there was never any stenosis of the canal (Fig. 5). However, following the removal of advanced lesions involving the concha and the entire circumference of the canal, there may be some tendency for stenosis to occur (Fig. 6). Therefore, it is advisable to keep the canal distended during and immediately after healing. For this purpose petrolatum gauze wicks or catheter tips may be used.

Cancers involving the canal and extending into the middle ear and around the mastoid and styloid processes have been followed out by the chemosurgical

technique, using long, slender scalpels and forceps. Unfortunately, however, the lesions of this type encountered in this series all have been so advanced that the patients succumbed either to carcinomatous invasion of deeper structures or to metastasis.

Difficulty due to hemorrhage is not encountered during the chemosurgical treatment of carcinomas of the ear, with the exception of those extending into the region of the superficial temporal or external carotid arteries. If, during the excision of the layers of fixed tissue, there is bleeding, it usually can be controlled by the application, under pressure, of a small piece of gauze impregnated with the zinc chloride fixative. If bleeding should occur during separation of the final layer of fixed tissue, a suture-ligature may be required.

Fig. 3.—*A*, Squamous-cell carcinoma, grade 2 malignancy, of Group D (average diameter, 3 cm. or more). The lesion began in the concha but extended through the full thickness of the ear (*B*). *C*, Granulation tissue thirteen days after the start of treatment. *D*, Healed lesion after two months. There was no cancer present when the patient died of other disease after two and one-quarter years.

THERAPEUTIC RESULTS IN CASES OF SQUAMOUS-CELL CARCINOMA OF THE EAR

A total of fifty-two patients with squamous-cell carcinomas of the ear was chemosurgically treated. The extent of the lesions ranged from very early to extremely advanced. Thirty per cent of the cancers were recurrent following previous surgical or radiation treatment.

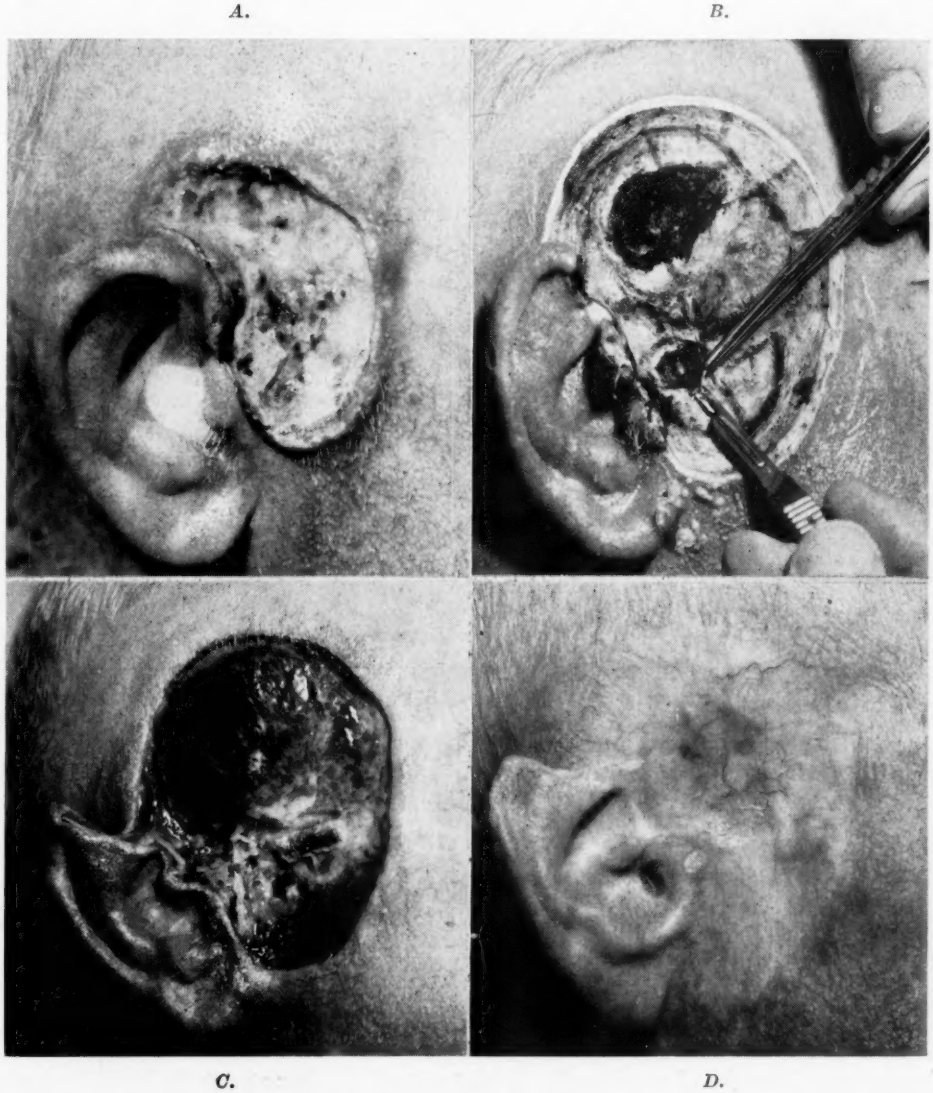


Fig. 4.—*A*, Squamous-cell carcinoma, grade 3 malignancy, of Group D (average diameter, 3 cm. or more). The lesion began in the preauricular region, and despite repeated roentgen ray and radium treatments over a period of one and one-half years, it extended back into the pinna but more extensively into the scalp and cheek. *B*, Lesion under treatment after one week, showing white, fixed tissue with markings used to orient specimens removed for microscopic study. The two black areas contained cancer and were still under treatment: the lower area is shown in process of excision. A cancer-free plane was reached on the eighth day. The layer of fixed tissue, 1 to 2 mm. thick, which at this stage was adherent was removed seven days later. *C*, Granulation tissue on the seventeenth day showing exposed zygoma. *D*, Healed lesion. The patient remains free of cancer after six years.

Primary Lesion.—Of the fifty-two patients in this series, fifty were followed for six months or more. In this group of fifty patients, the primary squamous-cell carcinoma was eradicated in forty-six (92 per cent).

The four cancers which were not eradicated were far advanced. One was a massive carcinoma with a malignancy of grade 3; it eroded through the temporal bone into the transverse venous sinus. The second was a deep-seated cancer with a malignancy of grade 3, involving the ear canal along with the temporomandibular joint and surrounding structures. The third was a massive carcinoma with a malignancy of grade 2, which arose in the canal. There was also cervical metastasis; therefore no drastic effort was made to remove a recurrent mass which extended into the middle ear. The fourth lesion not eradicated was a carcinoma which arose in the region of the middle ear. It extended outwardly in the ear canal and inwardly around the great vessels into the oropharynx.

A *B.* *C.*

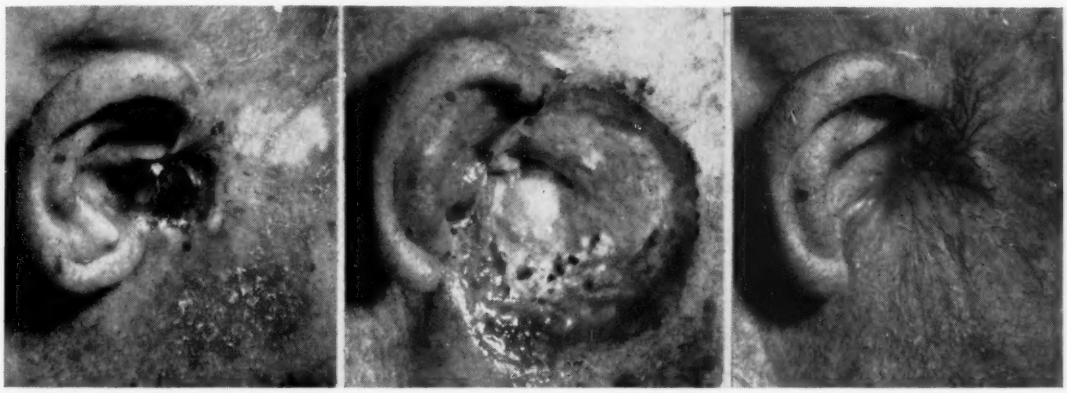
Fig. 5.—*A*, Squamous-cell carcinoma, grade 4 malignancy, of Group D. The lesion began on the antihelix and in eighteen months destroyed the ear. *B*, Granulation tissue four weeks after start of treatment showing mastoid process, which was exposed because of cancerous invasion of the periosteum. The necrotic layer of bone sloughed off one month later. *C*, Healed lesion, showing patent canal. The patient was kept under observation by his family doctor, and no evidence of cancer was found for nearly two years when metastasis in a deep cervical node was stated to have suddenly made its appearance. When he returned to the hospital the node was too large to justify radical dissection in consideration of the patient's advanced age.

In general, it may be stated that any carcinoma of the external ear may be removed by the chemosurgical method if there is not actual involvement of underlying vital structures, such as the brain with its venous sinuses, the carotid, or jugular vessels.

End Results After Six Months or More.—While end results after six months are of limited value for the comparison of the results with those obtained by other methods, they form a fairly accurate expression of the ultimate outcome. This is so because residual cancer, if present after chemosurgical treatment,

usually makes itself evident well within the six-month period because it is not deeply buried in a surgical incision, nor is it kept in abeyance by an atrophic radiation scar. Moreover, metastases usually become evident before a period of six months has passed.

The fifty-two cases of squamous-cell carcinoma were divided into "indeterminate" and "determinate" groups following the example of Martin, MacComb, and Blady.[5] The indeterminate group includes: (1) the cases of patients who died of intercurrent disease without evidence of recurrence and (2) those who were lost from observation without recurrence. The determinate group is composed of: (1) the cases of patients in whom unsuccessful results were obtained (the patients who have died of cancer, who have been lost from observation with cancer, or who are living with cancer) and (2) the cases of patients in whom successful results were obtained (the patients who remained free of cancer for six months or more).



A. *B.* *C.*

Fig. 6.—*A*, Basal-cell carcinoma, invasive histologic type, of Group D (average diameter, 3 cm. or more). The lesion began fourteen years previously on the tragus. It continued to spread back into the canal and into the ear lobe despite repeated treatments with radium, roentgen ray, and electrosurgical procedures. *B*, Granulation tissue sixteen days after the start of chemosurgical treatment. That the cancer had extended considerably more widely than would have been supposed from clinical examination is indicated by the size of the defect. The white area anterior to the canal is the articular process of the mandible. The branch of the facial nerve supplying the frontalis muscle was interrupted. Five months later an island of cancer, which apparently had been cut off from the main mass by some previous treatment, was discovered in the infra-auricular region. After two years no more cancer has appeared, but the diameter of the canal has been reduced to 1 millimeter (*C*).

In the fifty cases of squamous-cell carcinoma in the determinate group, the rate of cure after six months or more was 80 per cent (Table I).

Three-Year and Five-Year End Results.—An intensive follow-up program had as its goal the observation of every patient for at least five years. In this series only one patient was lost from observation.

In the three-year period successful results were obtained in 74.2 per cent of the thirty-one cases in the determinate group (Table I).

In the five-year period successful results were obtained in 64.3 per cent of the fourteen cases in the determinate group (Table I).

Effect of Size of Lesion on Prognosis.—The fifty lesions included in the determinate group in the six-month period were divided into four groups accord-

TABLE I. END RESULTS FOR SQUAMOUS-CELL CARCINOMA OF THE EAR AFTER PERIODS OF SIX MONTHS, THREE YEARS, AND FIVE YEARS

	SIX-MONTH PERIOD	THREE-YEAR PERIOD	FIVE-YEAR PERIOD
Total number of cases	52	35	19
Indeterminate group			
Patients dead from other causes without recurrence	1	4	5
Patients lost from observation without recurrence	1	0	0
Total number	2	4	5
Determinate group			
Total number	50	31	14
Unsuccessful results			
Patients dead from cancer present at time of death	10	8	5
Patients lost from observation with cancer	0	0	0
Patients living with cancer	0	0	0
Total number	10	8	5
Successful results			
Patients free from cancer for six months or more	40		
Patients free from cancer for three years or more		23	
Patients free from cancer for five years or more			9
Six-month end results			
Total number of cases with successful results divided by total number of determinate cases (40 ÷ 50)	80.0%		
Three-year end results			
Total number of cases with successful results divided by total number of determinate cases (23 ÷ 31)		74.2%	
Five-year-end results			
Total number of cases with successful results divided by total number of determinate cases (9 ÷ 14)			64.3%

This series includes the cases of all patients with histologically proved squamous-cell carcinomas, both early and advanced, previously untreated and recurrent, admitted to the Chemosurgery Clinic from Aug. 26, 1936, to Sept. 29, 1945, for the six-month group, from Aug. 26, 1936 to Jan. 10, 1943, for the three-year group, and from Aug. 26, 1936 to Feb. 14, 1941, for the five-year group.

ing to their average diameter: Group A, under 1 cm.; Group B, 1 to 2 cm. (Fig. 1); Group C, 2 to 3 cm.; and Group D, 3 cm. or more (Figs. 3 to 5). The measurements always refer to the size as clinically determined before treatment was begun rather than to the size as determined during the course of chemosurgical treatment.

As was to be expected, the rate of cure in Group A was high (100 per cent) but tapered off in the larger size groups (Table II).

Effect of Previous Treatment on Prognosis.—Thirty per cent of the fifty patients with squamous-cell carcinomas in the determinate group had received previous unsuccessful treatment by means of some surgical or radiation procedure either alone or in combination. Although it was possible to salvage

TABLE II. EFFECT OF SIZE OF SQUAMOUS-CELL CARCINOMA ON PROGNOSIS

GROUP	AVERAGE DIAMETER (CM.)	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
			NUMBER	PER CENT
A	Under 1	16	16	100.0
B	1 to 2	15	13	86.7
C	2 to 3	6	3	50.0
D	3 or more	13	8	61.5
All groups		50	40	80.0

53.3 per cent of the patients with recurrent lesions, the rate of cure was well below the 91.4 per cent attained in the group of patients who gave no history of previous treatment (Table III). The poorer prognosis in patients with recurrent lesions was due largely to the delay and the increase in extensiveness which occurred during the period of inadequate treatment.

TABLE III. EFFECT OF PREVIOUS TREATMENT OF SQUAMOUS-CELL CARCINOMA ON PROGNOSIS

	NUMBER OF PATIENTS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
Previously treated	15	8	53.3
Previously untreated	35	32	91.4

Effect of Histologic Grade of Malignancy on Prognosis.—The fifty squamous-cell carcinomas, upon classification on the basis of Broders' four grades of malignancy, were distributed as follows: grade 1, 24 per cent; grade 2, 48 per cent; grade 3, 20 per cent; and grade 4, 8 per cent.

In agreement with Broders' conclusions,[6] the prognosis in the present series was strongly affected by the grade of malignancy as indicated by the fact that the rate of cure was 91.7 per cent for lesions with a malignancy of grades 1 and 2 but dropped to 60 and 25 per cent for lesions with a malignancy of grades 3 and 4, respectively (Table IV). The reason for this drop in rate of cure was due largely to the greater tendency toward metastasis exhibited by cancers of higher malignancy.

TABLE IV. EFFECT OF HISTOLOGIC GRADE OF MALIGNANCY OF SQUAMOUS-CELL CARCINOMA ON PROGNOSIS

GRADE	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
1	12	11	91.7
2	24	22	91.7
3	10	6	60.0
4	4	1	25.0

Effect of Metastasis on Prognosis.—The prognosis in cases of carcinoma of the ear is much worse in those in which cervical metastasis has occurred. Thus, in the fifty patients in the determinate group there were seven who eventually developed cervical metastases, and all of these patients died from cancer. In contrast, in the group of forty-three patients who did not develop metastases there was a rate of cure of 93 per cent (Table V).

The metastases were diagnosed at the beginning of treatment in three cases, while in four others they were found at checkup examinations. There

TABLE V. EFFECT OF METASTASIS ON PROGNOSIS

	NUMBER OF PATIENTS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
With metastasis	7	0	0
Without metastasis	43	40	93

were four patients who at the onset of treatment had enlarged regional nodes which later returned to normal upon removal of the infected primary lesion.

No prophylactic neck dissections were done in this series, but a policy of close postoperative observation was followed. Unfortunately, the four patients who developed nodes after removal of the primary lesion failed to return as soon as requested; therefore, the metastases became extensive. In all of the patients who developed metastases there had been large primary cancers of higher than usual malignancy (two each were classified as grades 2 and 3 and three were classified as grade 4). In view of these circumstances it probably would be wise to consider prophylactic dissection of the cervical nodes for patients having large, highly malignant, primary cancers. This would seem to be indicated particularly in patients who cannot be relied upon to return regularly for checkup examinations.

In three patients of this series surgical and chemosurgical dissection of metastatic cervical nodes was carried out, while in six patients palliative roentgen therapy was given either alone or in conjunction with the aforementioned surgical procedures. These procedures were of definite temporary benefit and they made it possible to delay the fatal termination for as long as three years.

Effect of Site of Origin on Prognosis.—The fifty squamous-cell carcinomas in patients in the determinate group arose in the seven regions which are listed in Table VI. A majority (twenty-eight) of the lesions were located on the outer rim of the ear and on the anterior surface, and in these locations the prognosis was uniformly good; the rates of cure were as follows: helix and lobe, 100 per cent; antihelix and crura, 93.8 per cent; and concha, 100 per cent).

The rates of cure were somewhat lower for cancers arising on the posterior surface of the ear (66.7 per cent), in the postauricular region (75 per cent), and in the preauricular and tragal regions (75 per cent). The lowest rate of cure was for lesions arising in the canal and deeper structures; none of the four

TABLE VI. EFFECT OF SITE OF ORIGIN OF SQUAMOUS-CELL CARCINOMA ON PROGNOSIS

SITE	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
Helix and lobe	10	10	100.0
Antihelix and crura	16	15	93.8
Concha	2	2	100.0
Canal and deeper structures	4	0	0.0
Posterior surface	6	4	66.7
Postauricular region	8	6	75.0
Preauricular and tragal region	4	3	75.0
All sites	50	40	80.0

in this group were cured. In general, the more medial the site of origin the worse was the prognosis. Conversely, the nearer to the outer rim of the ear the better the prognosis tended to be. This tendency was in part due to the fact that the lesions arising more medially would more quickly erode into underlying vital structures and in part due to the richer lymphatic supply in the deeper structures with the consequent greater tendency toward metastatic spread. Most of the lesions which metastasized arose on the posterior surface of the ear or in the adjacent postauricular region; these usually soon invaded the posterior-auricular groove, and in this location any movement of the ear strongly traumatized the cancer. This trauma doubtless increased the tendency for metastasis to occur.

The poor results with the four lesions arising in the canal or deeper structures were ascribed to the fact that in three metastasis had occurred, while in the fourth the carcinoma, which arose in the region of the middle ear, had spread medially to the oropharynx. There is no reason why less advanced lesions of the canal should not respond well to chemosurgical treatment.

THERAPEUTIC RESULTS IN CASES OF BASAL-CELL CARCINOMA OF THE EAR

A consecutive series of fifty-five patients with basal-cell carcinomas of the ear was treated chemosurgically. In this group, 25.5 per cent of the cancers were recurrent following previous surgical or radiation treatment. There was no instance of metastasis.

End Results After Six Months or More.—Of the fifty-five patients with basal-cell carcinoma followed for six months or more, fifty-one were in the determinate group. Of this group, forty-seven were successfully treated, so the rate of cure was 92.2 per cent (Table VII).

Treatment was unsuccessful in four patients. Two of these had extensive involvement of the temporal bone, so that complete removal was not feasible. Two others had lesions arising deep in the canal and they could not be removed completely because of extensive involvement in the vicinity of the middle ear and deeper structures.

Three-Year and Five-Year End Results.—In the series of thirty-five patients followed for three years or more, there were thirty-one in the determinate group. In the latter group there were twenty-seven successfully treated patients; therefore, the rate of cure after three years or more was 87.1 per cent (Table VII).

There were twenty-five patients followed for five years or more and of these twenty-one were in the determinate group. Of those in the latter group, seventeen were successfully treated, so the rate of cure after five years or more was 81 per cent (Table VII).

It will be noted that there were four failures in the six-month group, four in the three-year group, and four in the five-year group. This circumstance was due to the fact that all of the failures occurred early in the course of the project. Since the total number of cases in the groups followed for the longer terms was smaller, there is in them a consequent lower rate of cure. In the group of thirty-eight patients with basal-cell carcinoma of the ear treated during the past eight years, there have been no failures.

TABLE VII. END RESULTS FOR BASAL-CELL CARCINOMA OF THE EAR AFTER PERIODS OF SIX MONTHS, THREE YEARS, AND FIVE YEARS

	SIX-MONTH PERIOD	THREE-YEAR PERIOD	FIVE-YEAR PERIOD
Total number of cases	55	35	25
Indeterminate group			
Patients dead from other causes without recurrence	3	3	3
Patients lost from observation without recurrence	1	1	1
Total number	4	4	4
Determinate group			
Total number	51	31	21
Unsuccessful results			
Patients dead from cancer present at time of death	3	3	3
Patients lost from observation with cancer	1	1	1
Patients living with cancer	0	0	0
Total number	4	4	4
Successful results			
Patients free from cancer for six months or more	47		
Patients free from cancer for three years or more		27	
Patients free from cancer for five years or more			17
Six-month end results			
Total number of cases with successful results divided by total number of determinate cases (47 ÷ 51)	92.2%		
Three-year end results			
Total number of cases with successful results divided by total number of determinate cases (27 ÷ 31)		87.1%	
Five-year end results			
Total number of cases with successful results divided by total number of determinate cases (17 ÷ 21)			81.0%

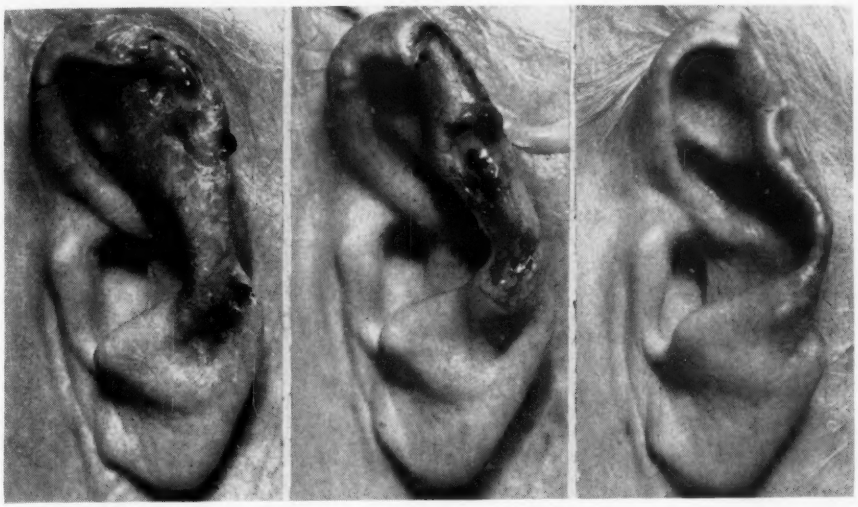
This series includes the cases of all patients with histologically proved basal-cell carcinomas, both early and advanced, previously untreated and recurrent, admitted to the Chemosurgery Clinic from June 26, 1936 to Sept. 29, 1945, for the six-month group, from June 26, 1936 to April 15, 1943, for the three-year group, and from June 26, 1936 to Oct. 7, 1940 for the five-year group.

TABLE VIII. EFFECT OF SIZE OF BASAL-CELL CARCINOMA ON PROGNOSIS

GROUP	AVERAGE DIAMETER (CM.)	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
			NUMBER	PER CENT
A	Under 1	14	14	100.0
B	1 to 2	18	18	100.0
C	2 to 3	6	5	83.3
D	3 or more	13	10	76.9
All groups		51	47	92.2

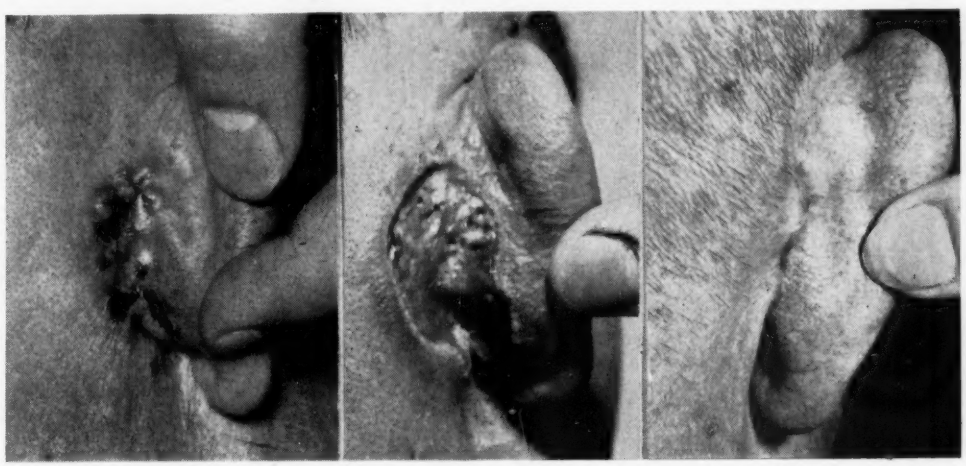
Effect of Size of Lesion on Prognosis.—The fifty-one basal-cell carcinomas in the determinate group in the sixth-month period were fairly evenly distributed in the four groups as regards size of the primary lesion (Table VIII). No failures occurred in the treatment of lesions in the two smaller-sized groups. One

failure is listed in Group C (average diameter, 2 to 3 cm.), and three failures are listed in Group D (average diameter, 3 cm. or more). (Examples of lesions in Group D are shown in Figs. 6 to 8.)



A. *B.* *C.*

Fig. 7.—*A*, Mixed basal- and squamous-cell carcinoma, of Group D. In addition there was a painful radiodermatitis from two courses of roentgen-ray therapy given ten years and six years before. *B*, Granulations after removal of fixed tissue including cartilage. *C*, Healed lesion. The patient remains free of cancer after five years.



A. *B.* *C.*

Fig. 8.—*A*, Basal-cell carcinoma of Group D. The lesion arose in the postauricular region and grew into the posterior-auricular fold and onto the posterior surface of the ear. Treatment with caustics had been ineffective. *B*, Granulation tissue after twelve days. *C*, Healed lesion showing linear scar. The patient remains free of cancer after three years.

In general, however, large size as such is not an appreciably deterrent factor because the microscopic control afforded by the chemosurgical method makes possible the eradication of very large cancers with all their irregular ramifications. It is more the degree of invasion of underlying vital and inaccessible structures that determines whether or not a successful result is to be obtained.

Effect of Previous Treatment on Prognosis.—Of the fifty-one patients in the determinate group in the six-month period, thirteen (25.5 per cent) had received previous surgical or radiation treatment. In this group with recurrent lesions the rate of cure was 76.9 per cent as compared to the 97.4 per cent in the group which had received no previous treatment (Table IX). The chief reason for the poorer prognosis in patients with recurrent lesions was the delay occasioned by the ineffective treatment.

TABLE IX. EFFECT OF PREVIOUS TREATMENT OF BASAL-CELL CARCINOMA ON PROGNOSIS

	NUMBER OF PATIENTS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
Previously treated	13	10	76.9
Previously untreated	38	37	97.4

The particular usefulness of the chemosurgical method in the treatment of recurrent and often otherwise hopeless cancer is demonstrated by the fact that over three-fourths of the patients with recurrent lesions were salvaged.

Effect of Histologic Grade of Malignancy on Prognosis.—The fifty-one basal-cell carcinomas were grouped according to their degree of invasiveness as determined by microscopic examination. Although there are borderline cases in which it is difficult definitely to classify the lesion as invasive or noninvasive, the majority can be placed readily in one or the other of these categories.

The invasive type exhibits slender strands of basal cells which often assume spindle shapes and which intrude themselves into the interstices of the normal tissues; there is often a strong stroma reaction. (Included in the group of invasive lesions are seven basal-cell carcinomas with some degree of keratinization, two transitional-cell carcinomas, and two mixed basal- and squamous-cell carcinomas.) On the other hand, the noninvasive type of basal-cell carcinoma is made up of regularly shaped cells which are packed closely in rounded or serrated clumps. These clumps are well demarcated from the surrounding stroma which is usually relatively sparse. (Only one lesion of this type exhibited keratinization, and one was a mixed basal- and squamous-cell carcinoma.)

In this series of fifty-one basal-cell carcinomas there were thirty-eight lesions of the invasive type (74.5 per cent). The rate of cure for these invasive lesions was 89.6 per cent. In contrast, the rate of cure for the thirteen noninvasive lesions was 100 per cent (Table X). The somewhat poorer prognosis associated with invasive carcinoma is due to the ingrowing, destructive nature of the neoplasm, with the consequent more frequent involvement of deep, vital structures. The good prognosis in the noninvasive type is due to the outgrowing,

TABLE X. EFFECT OF HISTOLOGIC GRADE OF MALIGNANCY OF BASAL-CELL CARCINOMA ON PROGNOSIS

	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
Invasive	38	34	89.6
Noninvasive	13	13	100.0

relatively nondestructive nature of the lesion; this type may reach a tremendous size and yet cause little destruction of the underlying structures.

It is in the highly invasive lesions that the chemosurgical method is of greatest advantage, because these lesions commonly send out irregular extensions which completely escape detection until located and followed to their terminations by means of repeated microscopically controlled excisions.

Effect of Site of Origin on Prognosis.—As with squamous-cell carcinomas, the basal-cell carcinomas arising on the pinna of the ear carry a better prognosis than those arising in more proximal portions of the ear. Thus, the twenty-one lesions which arose on the helix and lobe, in the concha, and on the posterior surface of the ear all were treated successfully (Table XI). On the other

TABLE XI. EFFECT OF SITE OF ORIGIN OF BASAL-CELL CARCINOMA ON PROGNOSIS

SITE	NUMBER OF LESIONS	SUCCESSFUL RESULTS	
		NUMBER	PER CENT
Helix and lobe	8	8	100.0
Antihelix and crura	–	–	–
Concha	7	7	100.0
Canal and deeper structures	2	0	0.0
Posterior surface	6	6	100.0
Postauricular region	16	15	93.8
Preauricular and tragal region	12	11	91.7
All sites	51	47	92.2

hand, the lesions with a more proximal origin had a lower rate of cure (canal and deeper structures, 0 per cent; postauricular region, 93.8 per cent; and preauricular and tragal region, 91.7 per cent). The reason for the poorer prognosis in the more proximal lesions is the closer proximity to underlying vital or inaccessible structures, the involvement of which renders a cure impossible. For example, one of the lesions which arose deep in the canal or in the middle ear had eroded the bone all around these structures. Although the external portion which extended for 15 cm. in the periosteum of the temporal and parietal bones was successfully removed by means of numerous microscopically controlled excisions, the deep-seated portion which eroded the bone recurred. Another deeply invasive lesion of the canal recurred, as did two far-advanced cancers which arose in the preauricular and postauricular regions, respectively and extensively invaded the temporal bone.

THERAPEUTIC RESULTS IN PRECANCEROUS LESIONS OF THE EAR

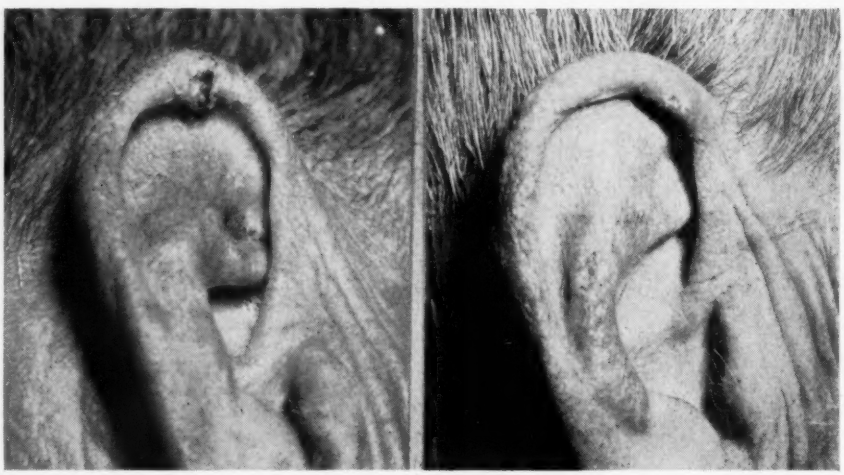
The chemosurgical method is often of value in the treatment of precancerous lesions of the ear because the microscopic control inherent to the technique makes complete removal certain and also detects early cancerous changes which may not be clinically discernible.

Senile Keratoses.—The most common precancerous lesions of the ear are senile keratoses. These are most often found on the portions of the ear most exposed to the rays of the sun, particularly on the helix (Fig. 9) and antihelix. Including two cutaneous horns and one squamous-cell papilloma, there was treated a total of twenty-six senile keratoses. To twenty-two of these the zinc chloride fixative was applied following preparation with dichloracetic acid,

and in these the diagnoses were microscopically confirmed. Four lesions, which from clinical appearance were quite certainly inactive, were cauterized with dichloracetic acid.

The patients have been followed for variable periods up to seven and one-half years and no instance of recurrence or malignant change has been observed.

Seborrheic Keratoses.—Although less common on the ear and less likely to undergo malignant change, seborrheic keratoses were treated with the chemosurgical technique in five patients and with dichloracetic acid alone in two patients. No recurrences or malignant changes have appeared during observation periods up to four years.



A. *B.*

Fig. 9.—*A*, Senile keratosis. *B*, Healed lesion after chemosurgical excision. The microscopic sections showed much precancerous, epithelial hyperplasia but no actual neoplasia.

Radiation Ulcers.—The chronic ulcers which occasionally follow intensive roentgen or radium irradiation of lesions on the ear may be classified as precancerous lesions. They may be advantageously treated by the chemosurgical method because the technique allows study of the tissues for possible neoplasia and also enables the efficient removal of the damaged tissues so that prompt healing may occur.

Five patients with radiation ulcers were treated. In three the ulcers healed promptly and there has been no recurrence or malignant change. One patient died of other causes two weeks after treatment. In one patient the radiation ulcer, which was so severe that the entire ear had sloughed off, has not healed after two months due to the slow separation of necrotic bone.

DISCUSSION

One important by-product of the work on the chemosurgical method has been the clear demonstration of the frequent occurrence of irregular, small-caliber, clinically undiagnosed outgrowths from the main cancerous mass. This characteristic of cancer has been well illustrated by means of reconstructions by Lathrop[7] and Limberg.[8]

In cancer of the ear these unsuspected outgrowths are frequently encountered. By means of the microscopically controlled excision, characteristic of the chemosurgical method, each of these extensions may be followed accurately to its termination. This explains the great reliability of the method and also its conservatism.

The results obtained with the chemosurgical treatment of cancer of the ear compare favorably with those obtained with other methods. The best previously published series as regards adequate numbers, adequate statistical presentation, and excellence of results is that of Magnusson[9] of the *Radiumhemmet* in Stockholm. From his protocols it was determined that at three years the rate of cure for carcinoma of the ear was 76.2 per cent. In the present series the rate of cure at three years for basal- and squamous-cell carcinoma was 80.6 per cent. This record was attained despite the fact that in this series recurrent lesions constituted 32.3 per cent of the total whereas in Magnusson's series only 22.1 per cent of the lesions were recurrent. The distribution of the lesions as regards size was essentially the same in both series.

The conservatism of chemosurgical excision of cancer of the ear is important if plastic reconstruction is contemplated. Any portion of the ear which can be preserved is likely to be useful in this organ in which cartilaginous support is so important. Moreover, following chemosurgical treatment the tissues are healthy and well vascularized and do not present the difficulties sometimes encountered with irradiated tissues.

Since all cartilage damaged in the process of chemosurgical treatment is promptly removed there is no danger of perichondritis and intractible ulceration such as sometimes follows radiation therapy of cancer of the ear.

Lesions recurrent after roentgen or radium therapy (Fig. 7) constitute prime indications for chemosurgery because they are notoriously insensitive to further irradiation and are difficult to excise surgically because their exact extent is difficult to estimate accurately.

There was no operative mortality in this series. One patient died from coronary thrombosis, four days after treatment, and one died from hemorrhage, two months after treatment, due to carcinomatous invasion of the jugular vein. In neither case could these deaths be attributed to the chemosurgical procedures. In consideration of the advanced age and poor health of many patients with cancer this essential lack of operative mortality is a definite advantage.

Since a special clinic with specially trained personnel is essential to the most effective use of the chemosurgical technique, it is suggested that the method had best be practiced as a specialty.

SUMMARY AND CONCLUSIONS

The chemosurgical technique as used in the excision of cancer of the ear is described, and the therapeutic results in a series of 107 cases are analyzed.

The rates of cure in the series of patients with squamous-cell carcinoma of the ear were: 80 per cent at six months or more, 74.2 per cent at three years

or more, and 64.3 per cent at five years or more. The primary lesion was eradicated in 92 per cent of the patients.

The rates of cure in the series of fifty-five patients with basal-cell carcinoma of the ear were: 92.2 per cent at six months or more, 87.1 per cent at three years or more, and 81 per cent at five years or more.

The reliability and the conservatism of the method are both due to the systematic microscopic control of excision afforded by the chemosurgical technic.

REFERENCES

1. Mohs, F. E., and Guyer, M. F.: Pre-excisional Fixation of Tissues in the Treatment of Cancer in Rats, Cancer Research **1:** 49, 1941.
2. Mohs, F. E.: Chemosurgery: A Microscopically Controlled Method of Cancer Excision, Arch. Surg. **42:** 279, 1941.
3. Mohs, F. E.: Chemosurgical Treatment of Cancer of the Lip: A Microscopically Controlled Method of Excision, Arch. Surg. **48:** 478, 1944.
4. Mohs, F. E.: Chemosurgical Treatment of Cancer of the Nose: A Microscopically Controlled Method, Arch. Surg. **53:** 327-344, 1946.
5. Martin, H., MacComb, W. S., and Blady, J. V.: Cancer of the Lip, Ann. Surg. **114:** 341, 1941.
6. Broders, A. C.: Epithelioma of the Ear; A Study of 63 Cases, S. Clin. North America **1:** 1401, 1921.
7. Lathrop, T. G.: The Morphology of Certain Neoplasms as Demonstrated by Reconstructions, Thesis for Doctorate in Medicine, University of Wisconsin Medical School, 1940.
8. Limberg, A. W.: Clinical Applications of Chemosurgery, Thesis for Doctorate in Medicine, University of Wisconsin Medical School, 1946.
9. Magnusson, A. H. W.: Skin Cancer. A Clinical Study With Special Reference to Radium Treatment, Acta radiol., supp. 22, p. 1, 1935.

SUCCESSFUL SUTURE OF THE ABDOMINAL AORTA FOR ARTERIOVENOUS FISTULA

LIEUTENANT COLONEL NORMAN E. FREEMAN* AND LIEUTENANT COLONEL AMBROSE H. STORCK,† MEDICAL CORPS, ARMY OF THE UNITED STATES

(From the Vascular Surgical Center, DeWitt General Hospital, Auburn, Calif.)

ARTERIOVENOUS fistula involving the abdominal aorta and vena cava is rare since patients generally succumb to the initial massive hemorrhage. Makins[1] reported two patients who survived wounds of the abdominal aorta for several weeks. Even if the patient recovers from the initial loss of blood, the short-circuiting of the circulation immediately places such a strain on the heart that early cardiac failure occurs.

Pemberton, Seefeld, and Barker[2] have recently reported the successful repair of the abdominal aorta for an arteriovenous fistula. In a review of the literature they were unable to find any previously reported case in which the patient had survived a reasonable length of time after surgical repair to furnish evidence that the operation had been successful. The present case, which was briefly reported in discussion of their paper, is apparently the second patient in whom a successful repair of the abdominal aorta has been performed.

CASE REPORT

The patient‡ was a 25-year-old infantry soldier who was wounded on Okinawa May 14, 1945. A 25-caliber bullet entered the abdomen three inches below the ensiform cartilage just to the right of the midline and passed out through the back at the level of the second lumbar vertebra. He was immediately paralyzed below the waist. A laparotomy was performed on the day of injury and a large retroperitoneal hematoma was found. The patient stated that he was told that numerous veins were tied off. The abdomen was closed without drainage. Ten days after injury the patient was transferred to another hospital and roentgenograms were taken which disclosed several fracture lines in the spinous process of the second lumbar vertebra, radiating through the lamina without displacement or separation. On the fifteenth day after injury, a laminectomy was performed and the comminuted fragments of the spine at the first and second lumbar vertebrae and the lamina of the second lumbar vertebra were removed. The underlying dura was found to be compressed and lacerated and three of the roots were found to be severed. Following this operation there was considerable return of function in the lower extremities. On the fifth postoperative day, he developed swelling of the right leg, and a diagnosis of thrombophlebitis was made. The swelling subsided in a few days.

Six weeks after the original injury, the patient complained of some epigastric pain and, on examination, a pulsating mass with intense thrill was found to be present in the upper abdomen. A diagnosis of aneurysm of the abdominal aorta was made and the patient was evacuated to the Zone of the Interior. Upon admission to the Debarkation Hospital, it was noted that the blood pressure was 150/60. The hemoglobin was 72 per

Received for publication, June 19, 1946.

*From the Department of Surgery, University of California Medical School, San Francisco, Calif.

†From the Department of Surgery, Tulane Medical School, New Orleans, La.

‡This patient was originally admitted to the Vascular Surgical Section but, because of the associated lesion of the spinal cord, was transferred to the Neurosurgical Section. The urological problems which the case presented were managed by Lieutenant Colonel Donald C. Malcolm. We are also indebted to Lieutenant Colonel Richard B. Capps, Chief of the Medical Branch, for advice in the postoperative care.

cent and urine examinations showed some infection. At this time, some dilated veins over the abdominal wall were observed. The heart did not show enlargement either on physical examination or by x-ray examination. He was placed on tidal drainage for the urinary tract infection. The blood chemistry was essentially normal and the Kahn test was negative. He was transferred to the Vascular Surgical Center, DeWitt General Hospital, on Aug. 3, 1945. Examination at the time of admission revealed a pulsating mass in the epigastrium which was more prominent to the right of the midline. The superficial abdominal veins were dilated, as shown in Fig. 1.

Over the mass could be heard a continuous loud bruit which was accentuated during systole. The pulse rate was 96 and the blood pressure 152/96. The heart was not enlarged and there was no evidence of dilatation or engorgement of the neck veins. There was no dyspnea or orthopnea. Neurologic examination revealed a residual paraplegia, involving principally the motor components of the posterior tibial and common peroneal nerves on the right side with some involvement of the peroneal nerve on the left side. The sensory loss was small, being confined to a small area about the anus and scrotum on the right side. Venous pressure as measured in the right antecubital vein was 3 cm. of water. The lungs were clear and the liver edge was palpable at the right costal margin. Except for some vague discomfort in the right upper quadrant, there were no symptoms referable to the presence of the intra-abdominal aneurysm.

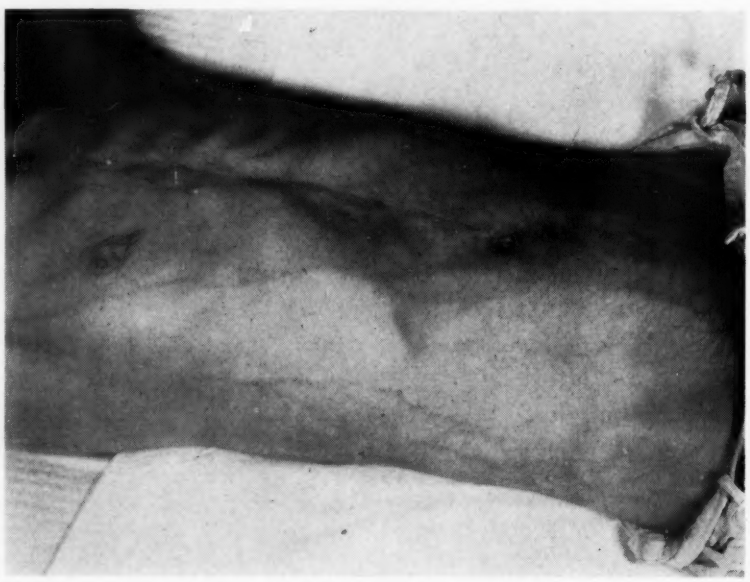


Fig. 1.

It was not possible to obliterate the thrill of the arteriovenous fistula by pressure in the epigastrium or right upper quadrant. The fact that the heart showed no evidence of marked strain, even three months after the development of an arteriovenous fistula, was interpreted as evidence that there was some interference with the free return of blood from the arterial to the venous side of the circulation. The absence of liver enlargement was evidence against involvement of the portal venous system. The dilatation of the superficial abdominal veins suggested involvement of the inferior vena cava. A diagnosis was made of arteriovenous fistula probably involving a branch of the abdominal aorta and either the vena cava or some tributary of this vein.

The patient was placed on the paraplegic ward, the bladder infection controlled by tidal drainage, and an attempt was made to have him increase his activities as much as was compatible with the residual neurologic lesions. His appetite improved and he started to regain some of the weight which he had lost. On September 15, four months after the

initial injury, the patient complained of some abdominal discomfort and vomited. Examination at this time disclosed the mass to be approximately 6 cm. in diameter. Both the pulsation and the thrill were more apparent. Gastrointestinal x-ray examination failed to reveal any extrinsic mass producing pressure upon the pylorus or duodenum. The cardiac consultant noted a definite increase in the size of the liver with an increase in the pulse rate, and felt that the patient was showing evidence of cardiac strain. Because of the possibility of cardiac damage and the increase in the size of the aneurysm, it was decided not to delay further, but to subject the patient to operation.

The operation was carried out under intratracheal ether-oxygen anesthesia. A right paramedian incision was made from the xyphoid to just below the umbilicus. Numerous dilated veins were encountered in the subcutaneous tissues. On opening the peritoneum, a large pulsating mass was found beneath the gastrohepatic omentum. A puckered scar was present near the border of the liver on the right side, which probably represented the point of entrance of the rifle bullet. The veins of the portal system did not appear to be dilated. The hepatic, common, and cystic ducts were readily visualized and appeared to be pushed forward by the pulsating mass which occupied the posterior aspect of the right upper quadrant. The aneurysm was under considerable pressure and at one point, below and slightly mesial to the gall bladder, the thrill of the arteriovenous fistula was most easily palpable. Compression at this point obliterated the thrill, but this maneuver appeared to produce an increase in the intra-aneurysmal pressure. The round ligament of the liver and some adhesions were divided. An attempt was made to visualize the artery entering the aneurysm by division of the gastrohepatic omentum. It was still not possible to localize the opening of the artery into the aneurysm. Only by pressure on the aorta at the hiatus of the diaphragm was it possible both to obliterate the thrill and to cause the aneurysmal sac to collapse. The aorta was, therefore, exposed at this point by dividing some of the fibers of the diaphragm and was encircled by a fine rubber catheter which was fitted to a Bethune tourniquet. Attempt at exposure of the aorta through the root of the mesentery beneath the transverse colon was unsuccessful because of the dilated veins in this region.

The peritoneum and transversalis fascia were then incised from within the abdomen just to the left of the midline, and by separation of these structures from the underlying muscles it was possible to expose the anterior surface of the psoas muscle and the vertebral column. By this procedure, the spleen, descending colon, pancreas, left kidney, and intestines were reflected to the right and the abdominal aorta was readily exposed as it lay on the anterior surface of the lumbar vertebrae. Many large veins were divided and ligated. The tissues about the aorta were thickened and edematous and there was some discoloration present indicative of old hemorrhage. The abdominal aorta was encircled by a segment of rubber tubing just proximal to the origin of the inferior mesenteric artery. It was then exposed just above the origin of the left renal artery and was again encircled by a piece of tubing. Compression of the aorta by this piece of tubing caused the sac to collapse. An additional section of tubing was placed about the left renal artery. With the proximal and distal aorta and left renal artery occluded, the inflammatory tissues surrounding the aorta at the site of the fistula were incised and the aorta was finally cut away from the aneurysm at this location. The opening into the aorta measured ½ inch in length. It was closed by a transverse running stitch of No. 000 Deknatel, which had previously been passed through sterile mineral oil. Bleeding from the sac was only moderate and was readily controlled by digital pressure. This opening was closed by a running stitch of No. 000 silk. At the conclusion of this procedure, the segments of tubing around the distal aorta, left renal artery, and then the proximal aorta were released. Good pulsation, expansile in character, was apparent in the aorta below the suture line. No bleeding took place. Two Penrose drains were inserted through a stab wound below the left costal margin into the region of the left lumbar gutter and the abdomen was closed. Fig. 2 illustrates the location of the fistula.

The operation lasted just under eight hours. During this time the patient received a continuous transfusion of 3,000 c.c. of whole blood and 500 c.c. of normal saline solution. When the abdominal aorta was occluded the blood pressure increased from 118/70 to 240/100. The pulse rate increased from 130 to 160, and the neck veins became markedly distended.

The tourniquet was left in place for one hour and forty minutes. Upon release of the rubber tubing, the systolic pressure dropped to 50, but within 30 minutes it rose to 110/80 and the pulse was 140. Immediately after operation, a strong femoral pulse was palpable and within one hour the extremities were warm and dry and the pulse at the wrist was of good volume. He was placed in an oxygen tent and suction was connected to an indwelling Levine tube. By the following morning, the abdomen was flat and peristalsis was present. The patient was conscious and alert. Because of persistent low blood pressure and a rapid weak pulse, he was given another blood transfusion, and penicillin and sulfadiazine were administered. Due to urinary suppression, the sulfadiazine was discontinued after the administration of 7 Gm. in the first thirty-six hours.

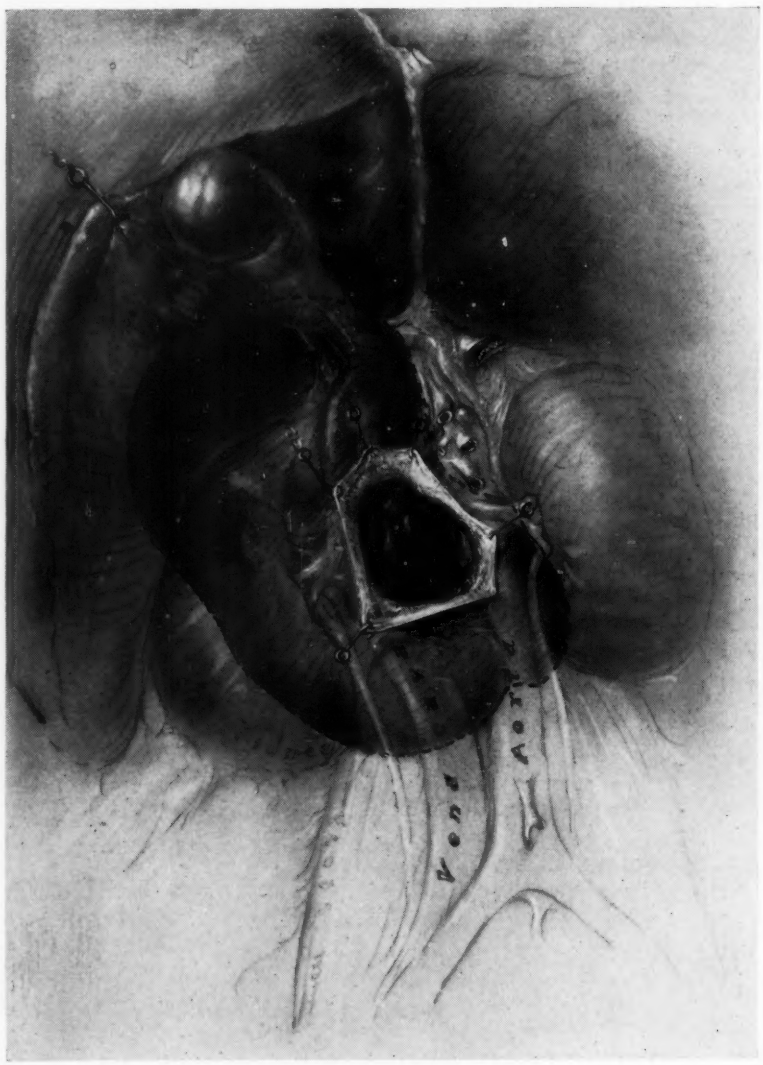


Fig. 2.

Impaired renal function presented a serious complication. During the first forty-eight hours, in spite of receiving 3,500 c.c. of 5 per cent glucose in water and 1,000 c.c. of 5 per cent glucose in saline solution, the patient passed only 200 c.c. of urine. The blood pressure following the transfusion increased to 160/90. The elevation of the nonprotein nitrogen following operation is shown in Table I.

TABLE I. CHEMICAL CONSTITUENTS OF THE BLOOD

DATE	NONPROTEIN NITROGEN	BLOOD UREA NITROGEN	CHLORINE	CARBON DIOXIDE	SERUM PROTEIN
July 27	33.7				
Aug. 14	34	18.7			7.1
Sept. 27		Operation			
Sept. 29	111.6		522	60.4	6.48
Sept. 30	116				
Oct. 1	116	80.9	541		5.39
Oct. 3	120	91	591		5.75
Oct. 5	107		572	59.3	6.48
Oct. 9	70.5		568	61.9	
Oct. 13	63.1				
Oct. 16	40.5				

For the first week, treatment consisted chiefly of continuous oxygen therapy, decompression of the upper gastrointestinal tract by nasal suction, and the moderate administration of intravenous fluids just sufficient to balance the amount lost through the gastrointestinal tract, kidneys, and insensible loss of water. Three days after operation, the venous pressure in the right antecubital vein was 12.6 cm. of saline solution. The patient was feeling well except for superficial erosions of the mouth and lips and lack of appetite. The blood pressure was consistently 170/80. Six days after operation, ophthalmologic examination revealed a remarkable generalized narrowing of the retinal arterioles throughout all divisions. In many of the vessels, there were variations in caliber indicative of focal spasm. No signs of sclerosis were noted, no exudation, hemorrhages or edema.

Fig. 3.

A diagnosis of acute retinal angiospasm was made. Because of persistent anorexia and sore mouth, the patient refused to eat so that on the tenth postoperative day a nasal tube was passed and he was given high caloric feedings by continuous drip for thirty-six hours; 1,500 c.c. of fluid containing approximately 1,800 calories were administered. He tolerated this feeding very well and his general condition improved rapidly. The nonprotein nitrogen of the blood dropped as the volume of urinary excretion increased. The wound healed without complications.

The day after operation, the patient noted that he was unable to dorsiflex the left foot. Neurologic examination showed that there was a definite increase in the neurologic disturbances noted prior to operation. In addition to the foot drop on the left side, the area of anesthesia had increased and there was a decrease in the bladder tone. For the first two months after operation, he complained of severe burning pain in both feet, but

this condition suddenly cleared up and there was a concurrent improvement in the motor power.

Evidence of renal damage persisted for several weeks with a constantly low specific gravity of the urine and persistent mild hypertension, and, even six weeks after operation, the ophthalmologic examination revealed moderate generalized narrowing and increased tortuosity of the retinal vessels. Excretory urograms demonstrated a good concentration on both sides without evidence of renal abnormality. As shown in Fig. 3, there was a defect in the laminae between the second and third lumbar vertebrae at the site of the original fracture.

From the location of the injury to the spinal column it seems likely that the laceration in the aorta was just below the origin of the right renal artery.

At the end of two months after operation he was able to stand, first with crutches, and finally was able to walk with the assistance of two canes. He was then transferred to another General Hospital. Eight months after operation it was reported that the patient had shown no evidence of recurrence of the fistula. He had recovered sufficiently from the spinal cord injury to be able to walk with the help of one cane.

COMMENT

The presence of a fistula between the abdominal aorta and vena cava leads, generally, to rapid heart failure and death. The absence of this complication in our patient was probably due to the intervention of a large aneurysmal sac between the compound vessels. The aneurysm, which lay behind the vena cava, displaced this structure forward and so compressed it as to hinder the ready flow of blood back to the right heart. The dilatation of the superficial abdominal veins observed before operation is in keeping with this explanation. It is possible that the onset of swelling of the right leg noted ten days after injury was due to interference of return flow of blood from the lower extremities rather than to an attack of thrombophlebitis.

The increase in the paralysis of the pelvic structures and lower extremities following operation was not surprising in view of the fact that the abdominal aorta was completely occluded for 105 minutes. Paralysis of the hindquarters has been observed in dogs by Blalock and Park[3] after complete occlusion of the aorta for a period of forty to fifty-five minutes. Whether the neural damage in our patient was due to impaired circulation to the spinal cord and cauda equina or due to temporary ischemia of the distal nerves would be hard to say, but the involvement of the nerves to the bladder suggests the former explanation. The rapid improvement which was observed two months after operation indicates a favorable prognosis.

The second postoperative complication was the temporary suppression of kidney function associated with hypertension. This complication was probably due to the renal ischemia produced by occlusion of the abdominal aorta above the renal arteries. It was associated with marked vasospastic changes in the eye grounds and nitrogen retention. With resumption of renal function at the end of two weeks, this hypertension subsided. The final urine concentration test, which was done two months after operation, showed an ability to concentrate to 1.018. The excretory urogram was also quite satisfactory, but it is quite possible that some permanent damage to the kidneys has been sustained. In the case reported by Alexander and Byron[4] on resection of a segment of the thoracic aorta, hypertension with severe retinal angiospasm, exudates, and hemorrhages proved a late serious complication. Persistent

hypertension with cardiac hypertrophy was also noted in the case reported by Pemberton, Seefeld, and Barker.[2]

At the time of operation considerable difficulty was experienced in locating the arterial communication with the fistula. Reflection of the duodenum with exposure of the anterior surfaces of the aorta and vena cava was the method of exposure employed by Pemberton and associates but the aneurysmal sac in their patient lay to the left of the aorta. Since in our patient the sac appeared to lie between the aorta and the vena cava this approach could not be used. It was only after retroperitoneal exposure of the anterior surface of the psoas muscle and the lumbar vertebrae through displacing the abdominal contents from the left lumbar gutter that the abdominal aorta could be readily exposed. It was then possible to visualize the entire length of this structure from the diaphragm to its bifurcation.

Transvenous suture of the opening between the aorta and vena cava was used by Pemberton and co-workers. This technique is known as the Matas-Bickham[5] operation. Although frequently valuable, it has the disadvantage of not permitting inspection of the entire arterial wall. Arterial aneurysms have been known to develop after this procedure if there happens to be an additional weakened point in the arterial wall. Closure of an arteriovenous fistula leads to a marked increase in blood pressure within the artery at the site of the fistula.[6] If the wall close to the former communication is defective it may give way, leading to the formation of an aneurysm. Complete dissection of the artery from the fistula permits thorough examination so that other damaged portions of the wall will not escape notice. In a series of cases to be reported[7] we have found it useful to excise the damaged portion of the arterial wall and close the defect transversely.

SUMMARY

The present case is the second successful suture of the abdominal aorta for an arteriovenous fistula to be reported. A complicating factor was the partial paraplegia resulting from concurrent gunshot wound of the spine. Operative approach to the abdominal aorta through the retroperitoneal space was employed. Increase in the extent of the neurologic damage and temporary renal failure with hypertension and retinal angiospasm were noted in the postoperative period.

REFERENCES

1. Makins, G. H.: Gunshot Injuries to the Blood Vessels, Bristol, 1919, John Wright and Sons, Ltd., p. 119.
2. Pemberton, J. deJ., Seefeld, P. H., and Barker, N. W.: Traumatic Arteriovenous Fistula Involving the Abdominal Aorta and the Inferior Vena Cava, Ann. Surg. **123**: 580, 1946.
3. Blalock, A., and Park, E. A.: The Surgical Treatment of Experimental Coaretation (Atresia) of the Aorta, Ann. Surg. **119**: 445, 1944.
4. Alexander, J., and Byron, F. X.: Aortectomy for Thoracic Aneurysm, J. A. M. A. **126**: 1139, 1944.
5. Matas, R.: Some Experiences and Observations in the Treatment of Arteriovenous Aneurisms by the Intrasaccular Method of Suture (Endo-Aneurismorraphy) With Special Reference to the Transvenous Route, Ann. Surg. **71**: 403, 1920.
6. Freeman, N. E.: Direct Measurement of Blood Pressure Within Arterial Aneurysms and Arteriovenous Fistulas, SURGERY **21**: 646, 1947.
7. Freeman, N. E.: Arterial Repair in the Treatment of Aneurysms and Arteriovenous Fistulas With a Report of Eighteen Successful Restorations, Ann. Surg. **124**: 888, 1946.

EVALUATION OF THE BASAL VASCULAR TONE TEST AS AN INDICATION FOR SYMPATHECTOMY IN THE TREATMENT OF SURGICAL LESIONS OF THE MAJOR ARTERIES

CAPTAIN E. W. RECTOR, MEDICAL CORPS, ARMY OF THE UNITED STATES
(From the Vascular Surgical Section, DeWitt General Hospital, Auburn, Calif.)

IN THE treatment of patients with aneurysms, arteriovenous fistulas, and obliteration of major vessels following trauma, the degree of development of collateral circulation is often the deciding factor which determines the outcome. Although the mechanism of the formation of collaterals is still not fully understood, it is recognized that vasoconstriction, through activity of the sympathetic nervous system, may interfere seriously with the supply of blood to the part. Lumbar sympathectomy, repeated injections of procaine into the region of the paravertebral sympathetic ganglia to induce temporary paralysis of vasomotor tone, or the paravertebral injection of alcohol to produce a longer lasting vasomotor release have been advocated in the treatment of these arterial lesions. Sympathectomy has even been recommended by Learmouth[1] as a prophylactic measure in all cases in which ligation of the major artery to an extremity is anticipated.

It is well recognized that, after ligation of arteries in certain anatomic locations, the collateral blood supply is generally quite adequate to care for the metabolic needs of the tissues. For example, following ligation of the superficial femoral artery, the incidence of gangrene or vascular disturbances is minimal, whereas ligation of the popliteal artery is followed by a more serious disturbance of the peripheral circulation. The extent of development of collateral circulation in the presence of an arteriovenous fistula is admittedly better than that observed in the presence of a surgical lesion involving the artery alone. The location of the lesion and the physiologic reactions which it produces are, therefore, important factors in estimating the prognosis in any given case. Even given the same anatomic location and equal disturbance of the main arterial supply, a considerable variation is noted in the degree of vascular insufficiency from one patient to the next. These differences may be ascribed to variations in the facility with which the collateral circulation is developed. It has been shown both experimentally and clinically that paralysis of vasoconstrictor impulses facilitates the development of these collaterals. It is my belief that sympathectomy should be reserved for those patients in whom an increased vasomotor tone can be demonstrated. The question arises as to how best to select those patients for sympathectomy in whom increased vasomotor tone is preventing adequate development of collateral circulation.

The first attempt to study quantitatively the vasomotor tone in man was made by Brown.[2] He noted the ratio between the rise in mouth temperature and the rise in temperature of the extremities following the administration of

Received for publication, June 14, 1946.

typhoid vaccine. Morton and Scott[3] used anesthesia, either general, local, or spinal, and White[4] was the first to use paravertebral procaine injections in order to inhibit vasomotor tone. Gibbon and Landis,[5] by the use of heat applied to the unaffected extremities, obtained a rise in the temperature of the digits. Since vasoconstriction is a normal physiologic response to cold, these tests, although useful in determining the degree of organic arterial occlusion, do not serve to estimate the degree of vasoconstriction which is present. A normal individual, when exposed to a cold environment, will develop vasoconstriction and the skin temperature, especially of the extremities, will fall to a low level. Coller and Maddock[6] have called attention to this fact and have warned against using the term vasospasm for a normal physiologic reaction. After release of vasomotor tone in such a normal individual, either by typhoid vaccine, anesthesia, or reflex vasodilatation, the peripheral skin temperatures will rise to normal high levels. These tests then are useful simply in ruling out organic vascular occlusions. They do not tell the degree of vasomotor activity with which the patient is responding. Considerable differences are observed in the study of the peripheral skin temperatures in any group of patients when exposed to the same environmental conditions. These differences may be related to the basal metabolic rate.[6] White and Smithwick,[7] on the basis of skin temperature curves of individuals exposed to cold, have separated patients into "hot-handed" and "cold-handed" types. The possibility of using these variations in temperature of the digits on exposure to cold as an index to the vasomotor tone of the individual patient has been suggested by Naide and Säyen.[8] In an analysis of the results obtained in 172 patients with the vasodilatation test they were able to group their patients into various types depending upon the skin temperature responses which they observed. Subsequently,[9] they reported that it was necessary simply to observe the skin temperature response of the finger tips during the cooling period in order to classify patients into two basic groups of high and low vascular tone. They regarded the individual as having a high vascular tone "if the hands are cool (below 25° C.) fifteen minutes after the patient has been in a constant-temperature room at 20° C. unclothed except for a light gown. If, on the contrary, the hands remain warm (25° C. or above) after this same exposure, the patient is in a low vascular tone group."

According to the results obtained from this test, Naide and Säyen[9] analyzed the effectiveness of the development of collateral circulation in seventy patients with occlusion of the femoral or popliteal artery which resulted either from arteriosclerosis, thromboangiitis obliterans, or embolism. They noted that 88 per cent of the patients with a low-vascular tone developed an excellent collateral circulation following major arterial occlusion. On the other hand, in the patients with a high degree of vascular tone, only 34 per cent developed an adequate collateral circulation. Since the development of collateral circulation following surgical lesions of the major arteries is of prime significance in determining the ultimate outcome, it seemed to us that this test might afford a suitable guide to determine which of the patients should be subjected to sympathectomy. The present investigation has been carried out in an endeavor

to evaluate the significance of the "basal vascular tone" test described by Naide and Säyen[9] as an indication for sympathectomy in the treatment of surgical lesions of the major arteries.

There are clinical evidences of increased vasomotor tone such as cyanosis, sweating, and constricted veins which were used by Freeman and Montgomery[10] in the selection of cases with intermittent claudication for sympathectomy. These clinical signs of increased sympathetic tone were used in the present investigation to separate patients into two groups, those exhibiting high and those exhibiting low vasomotor tone. The results of the basal vascular tone test were then compared with the impression obtained on clinical examination of the patient. The ultimate outcome in each patient served to assess the validity of the test in comparison with the clinical impression. This outcome was based on the degree of circulatory impairment, shown particularly by intermittent claudication, which followed ligation of the major artery supplying the extremity.

PROCEDURE

Measurements of skin temperature were made with the aid of a galvanometer in a constant-temperature room at 20° C. and 40 per cent humidity. The tests were made in the early morning during the summertime when the environmental temperature was comfortably cool. The patients were in a basal resting state, having omitted breakfast. No smoking was allowed before taking the test. The digital skin temperature was measured at the start of the test and every ten minutes for the succeeding hour. The values of the skin temperature readings obtained thirty minutes after the patient was admitted to the constant-temperature room served as a final reading.

RESULTS

Studies were completed on forty-five patients suffering from surgical lesions of the major arteries. Of these, twenty-five patients were studied before operation on aneurysms or arteriovenous fistulas. An additional seventeen patients were studied after the main artery to the extremity had been ligated in the course of operations on arterial lesions. There were three patients who were studied in whom thrombosis of an artery had developed following trauma or in whom the major artery had been ligated shortly after injury. Of the forty-five patients, arterial repair was performed at the time of operation on the vascular lesion in eleven. In an additional three patients, it was found at operation that the major artery to the extremity was not the one involved. In these fourteen patients, although it was possible to compare the impressions derived from examination with the results of the test, it was not possible to judge the relative significance of the two methods of evaluation by subsequent events since the continuity of the main artery was not interrupted. In the remaining thirty-one patients, it was possible to compare impressions gained by clinical observations and the indications supplied by the basal vascular tone test and to judge the relative merits of the two methods by the final outcome.

The results of the test were in agreement with the clinical impression in thirty-two of the forty-five patients. Of the thirteen cases in which there was

disagreement it was possible by analysis of the end results in ten patients to compare the significance of the two methods of selection. Clinical judgment was found to be superior to evaluation by the basal vascular tone test in eight of the cases. According to the test, seven of these patients had normal or low vascular tone. Yet clinical signs indicated abnormal vasoconstriction. In several instances in which the test was clearly in disagreement with the clinical observations it was repeated, but the results were the same. In spite of the findings of the test, sympathectomy was performed in six of the seven patients with excellent results. In the remaining case sympathectomy was advised but was not accepted. Persistence of intermittent claudication in this case after excision of a superficial femoral arteriovenous aneurysm supported the belief that the collateral circulation was slow to develop.

The test for basal vascular tone proved to be superior to clinical appraisal in only two patients. In one of these individuals persistent symptoms of intermittent claudication suggested that sympathectomy should have been performed even though there was no clinical evidence of abnormal vasoconstriction. The other patient developed no symptoms referable to vascular insufficiency even though there was clinical evidence of increased vasomotor tone. The fact that the arterial lesion in this patient was situated in the midfemoral region may have facilitated the development of collateral circulation in spite of abnormal vasoconstriction.

In Table I is shown a summary of the significance of the methods employed in the determination of vascular tone in selection of cases for sympathectomy. Six patients who showed evidence of abnormal vasomotor tone by each test were not subjected to sympathectomy for various reasons. Vascular insufficiency persisted in these patients supporting the validity of the criteria. On the other hand, in four patients who also showed evidence of increased vasoconstriction and in whom the test indicated a high basal vascular tone, no symptoms of vascular insufficiency developed even though sympathectomy was

TABLE I

	VALIDATION BY SUBSEQUENT EVENTS		EVALUATION NOT POSSIBLE BECAUSE OF ARTERIAL REPAIR OR NONSIGNIFICANT ARTERY	TOTAL CASES
	YES	NO		
Basal Vascular Tone Test				
High, sympathectomy	12	--	8	20
High, no sympathectomy	6	4	2	12
Low, sympathectomy	--	6	2	8
Low, no sympathectomy	2	1	2	5
Total	20	11	14	45
Clinical Evidence of Vasoconstriction				
High, sympathectomy	18	--	10	28
High, no sympathectomy	6	4	2	12
Low, sympathectomy	--	--	--	--
Low, no sympathectomy	2	1	2	5
Total	26	5	14	45

withheld. It is probably significant that the mid-portion of the superficial femoral artery was involved in three of these four cases.

Sympathectomy was performed in no cases in which clinical signs indicated normal vasomotor reactions. In only one case did subsequent events fail to confirm the clinical impression.

DISCUSSION

Observations on vascular impairment following surgical lesions of the major blood vessels support the concept that abnormal vasoconstriction or increased vasomotor tone hinders the development of adequate collateral circulation. The majority of patients who presented clinical evidence of high vasomotor tone as shown by cyanosis, sweating, and constricted veins developed symptoms of vascular insufficiency unless they were subjected to sympathectomy. By comparison, those with a low or normal vasomotor tone appeared to develop collateral circulation spontaneously. An attempt to place the estimate of vasomotor tone on a quantitative basis by the use of a basal vascular tone test suggested by Naide and Säyen[9] has not been entirely successful when applied to healthy young males with traumatic lesions of the major arteries. Results of the basal vascular tone test were not in accord with the clinical impressions gained from examination of the patients in over one-third of the cases. Subsequent events appeared to demonstrate the validity of the clinical impression in comparison to the information obtained from basal vascular tone test. This apparent discrepancy may be due to the difference in the character of the material which formed the basis for the study described in this paper. Thirty-eight of the seventy patients studied by Naide and Säyen[9] had sustained occlusions of the femoral or popliteal arteries due to arteriosclerosis. All of the patients discussed in this paper were vigorous young individuals who had recently returned from the combat zone. The fact that 63 per cent of the patients whom they tested had a low vascular tone whereas 73 per cent of the patients in the series described here had a high vascular tone according to the test serves to emphasize the difference in the type of patients who were studied.

A second possibility lies in the fact that all of the patients herein reported had sustained local trauma to the blood vessels. This injury might well have set up some degree of segmental vascular spasm. These local vascular reactions might be quite independent of the general vasomotor reactions of the body. The basal vascular tone test depends upon the skin temperature responses of the hands on exposure to cold. The vascular responses to local injuries may affect only the vessels distal to the site of trauma.

Admittedly, it would be desirable to have some objective means by which the vasomotor tone could be estimated in the selection of patients with traumatic lesions of arteries for sympathectomy. Without such a test, decisions must be based upon clinical experience which, of necessity, must be extensive. In my experience, however, when judged on the basis of the end results obtained in patients with traumatic lesions of the major arteries, clinical evidence of abnormal vasoconstriction has been more satisfactory than the basal vascular tone test in the selection of patients for sympathectomy.

SUMMARY

Vasoconstriction appears to interfere with the development of collateral circulation following surgical lesions of major arteries. Sympathectomy is indicated in those patients in whom increased vasomotor tone is present. The basal vascular tone test of Naide and Säyen[9] was compared to the clinical impressions obtained on physical examination in forty-five patients who had sustained injuries to the major arteries. The validity of the test or clinical impression was judged by the subsequent course of events. The test was in agreement with the clinical findings in thirty-two of the forty-five patients. When there was disagreement, clinical judgment appeared to be superior to the test in the majority of cases. In order to explain the discrepancy between the results reported here and those of Naide and Säyen[9] it is suggested that abnormal vasoconstriction may be induced by local trauma and that this segmental arterial spasm may be quite independent of the general vasomotor tone.

I wish to express my sincere gratitude to Major Norman E. Freeman, chief of the vascular surgical section, for his assistance and guidance in preparing this study.

REFERENCES

1. Learmouth, J. R.: The Surgery of Blood Vessels, Edinburgh M. J. **47**: 225, 1940.
2. Brown, G. E.: The Treatment of Peripheral Vascular Disturbances of the Extremities, J. A. M. A. **87**: 379, 1926.
3. Morton, J. J., and Scott, W. J. M.: Methods for Estimating the Degree of Sympathetic Vasoconstriction in Peripheral Vascular Diseases, New England J. M. **204**: 955, 1931.
4. White, J. C.: Diagnostic Blocking of Sympathetic Nerves to Extremities With Procaine, J. A. M. A. **94**: 1382, 1930.
5. Gibbon, J. H., Jr., and Landis, E. M.: Vasodilatation in the Lower Extremities in Response to Immersing the Forearms in Warm Water, J. Clin. Investigation **11**: 1019, 1932.
6. Coller, F. A., and Maddock, W. G.: The Function of Peripheral Vasoconstriction, Ann. Surg. **100**: 983-992, 1934.
7. White, J. C., and Smithwick, R. H.: The Autonomic Nervous System, New York, 1941, The Macmillan Company.
8. Naide, M., and Säyen, A.: A Test for Vascular Tone in Humans and Its Application to the Study of Vascular Diseases With Special Reference to the Etiology and Prevention of Thrombophlebitis, Am. J. M. Sc. **207**: 606, 1944.
9. Naide, M., and Säyen, A.: The Primary Influence of Basal Vascular Tone on the Development of Postocclusive Collateral Circulation and in Selecting Patients for Sympathectomy, Am. J. M. Sc. **209**: 478, 1945.
10. Freeman, N. E., and Montgomery, H.: Lumbar Sympathectomy in the Treatment of Intermittent Claudication, Am. Heart J. **23**: 224, 1942.

THE FLUORESCIN WHEAL TEST FOR COLLATERAL CIRCULATION IN THE PREOPERATIVE EVALUATION OF PATIENTS WITH ANEURYSMS AND ARTERIOVENOUS FISTULAS

CAPTAIN THEODORE B. MASSELL, MEDICAL CORPS, ARMY OF THE UNITED STATES
(From the Vascular Surgical Section, DeWitt General Hospital, Auburn, Calif.)

INTRODUCTION

ANEURYSMS of major peripheral arteries, although rare in civilian practice, are frequently encountered in military surgery. Some lesions involve an artery alone but the majority are associated with an arteriovenous fistula. Quadruple ligation of the constituent arteries and veins and excision of the fistula are usually performed. Ischemia of the tissues distal to the ligation is prevented by adequate blood flow through collateral vessels. Consequently, it is important to have assurance, prior to operation, that the collateral blood supply is sufficient for the needs of the peripheral tissues.

CLINICAL OBSERVATION

It is possible to arrive at a general estimate of the state of the collateral circulation from the history and physical examination of the patient. The duration of the presence of the aneurysm is significant in that adequate collaterals are rarely present in less than two months after injury. It is important to distinguish simple arterial aneurysms from arteriovenous fistulas inasmuch as the latter condition is generally associated with a much more rapid and abundant development of collateral channels than is the former.

The textbooks on surgical anatomy describe the so-called safe and unsafe sites for arterial ligation. While the anatomic principles concerned are true, there is actually far more variation in the size and even the location of major arterial branches than is commonly recognized. Accurate localization of an aneurysm in relation to some important collateral branch, for instance the subscapular or profunda femoris artery, may often be achieved by arteriography.

As Holman[1] emphasized, the chief stimulus to the development of collateral circulation in the presence of an arteriovenous aneurysm is the ease of flow through the site of decreased resistance at the fistula. The larger the fistulous opening, the more developed will be the collateral flow. For any given anatomic location, compression of a large fistula causes a greater rise in diastolic blood pressure and more slowing of the pulse rate than that observed with a small communication. Weak or absent pulses and low oscillometric readings distal to an arteriovenous aneurysm, two or three months after injury, suggest a large fistula whereas normal pulses and full oscillations are associated with a small opening. Likewise intermittent claudication in a patient with a femoral or a popliteal arteriovenous aneurysm is suggestive of a large communication.

Received for publication, April 30, 1946.

MATAS-MOSZKOWICZ TEST

Although clinical observation alone provides a good estimate of the state of the collateral circulation, some more exact method is desirable in most cases. In 1914 Matas[2] described a test for collateral blood flow which he attributed to Moszkowicz. According to this technique the involved artery is compressed just above the aneurysm by a special clamp until all blood flow through the sac is abolished. With the extremity elevated, an Esmarch bandage is firmly applied from the distal part of the extremity up to the aneurysm. The limb is kept emptied of blood in this way for from five to ten minutes. Then, with the compressor maintained in place, the Esmarch bandage is rapidly removed and the limb is brought to the horizontal position. The blood returns to the toes or fingers until a flush is produced. If the collateral circulation is good the flush will reach the distal parts within one minute. If more than three minutes is required, arterial ligation is contraindicated.

In using the Matas-Moszkowicz test, the results have been variable and the significance in preoperative selection of cases has been questionable. Interpretation of the end point has varied with different observers. The compressor may slip as the position of the extremity is changed so that blood may flow through a supposedly occluded artery. On more than one patient one observer has found the collateral time to be less than one minute on one day, only to have another observer on the same patient find an interval of over three minutes a few days later.

FLUORESCIN WHEAL TEST

Recently, Neller and Schmidt[3] described a new technique for the evaluation of the circulation in patients suffering from peripheral vascular disease. They discovered that fluorescin, when injected intravenously, would cause brilliant fluorescence at sites of minute trauma in an area where the peripheral circulation was not severely impaired but that no fluorescence would appear if the circulation was inadequate to supply the normal metabolic needs of the tissues. Furthermore, they found that the area of fluorescence corresponded to the wheal component of triple response to injury described by Lewis.[4] These authors then used this test to determine the safe level for amputation of limbs with impending or early gangrene. Although Neller and Schmidt reported their results in only six cases, their method seemed applicable to a study of the collateral circulation in cases of aneurysms and arteriovenous fistulas.

The following technique was employed. The flow of blood through the main artery at the site of the aneurysm was first completely occluded by a modified Matas compressor. The completeness of the occlusion was verified by auscultation before and after the test since a compressor might be tight enough to obliterate the palpable thrill of an arteriovenous aneurysm and yet allow enough blood to pass to produce a readily audible bruit. On the other hand the head of the clamp should be sufficiently small so as not to obstruct important collateral vessels near the aneurysm. A modification of the Matas compressor, which has proved satisfactory, is illustrated in Fig. 1.

With the clamp maintained tightly in place over the aneurysm, a series of parallel scratches was made, at intervals of 6 to 8 cm. on both extremities from

the level of the clamp to the proximal phalanx of the great toe or the middle finger. Ten cubic centimeters of 10 per cent fluorescin in a buffered sodium carbonate solution were injected into the antecubital vein. The room was darkened and the extremities were examined by filtered ultraviolet light. The scratches became brilliantly fluorescent within a few minutes after injection of the dye. The time required for appearance of fluorescence was not significant. The criterion of circulatory adequacy was taken as the lowest level of wheal fluorescence.

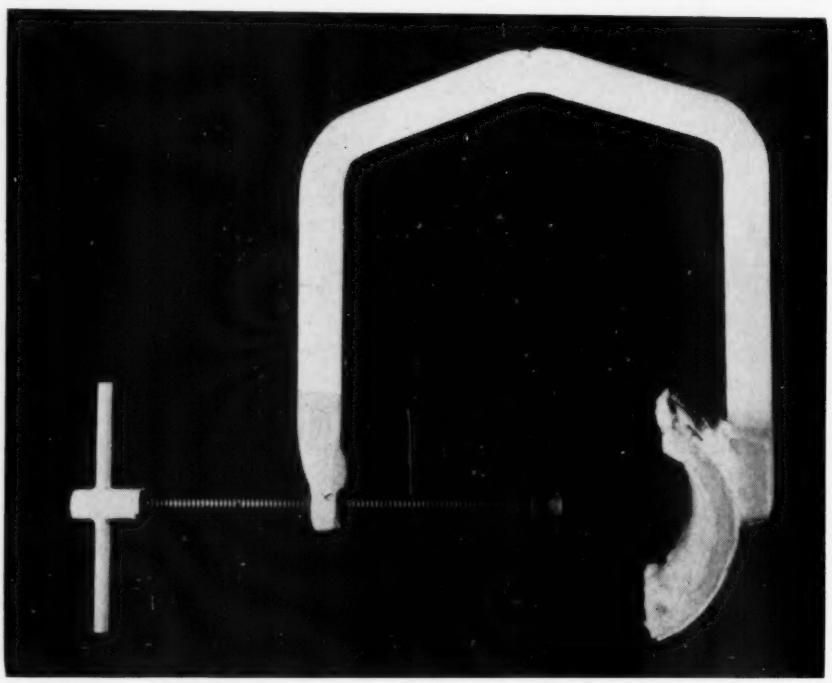


Fig. 1.—A modification of the Matas compressor. The plastic head is applied directly over the aneurysmal opening. A small head is used to avoid occlusion of collateral vessels in the vicinity. The curved surface of the opposite jaw tends to keep the clamp securely in place when the limb is moved.

At first this test was performed without a compressor on seven patients, each of whom had previously had a major peripheral artery ligated. The lower extremity was involved in six cases and the upper extremity in the seventh. None of the patients had gangrene but all had symptoms and signs of varying degrees of arterial insufficiency. Two had superimposed vasospasm. In order to establish a standard of normal circulation, the level of wheal fluorescence was tested simultaneously on the opposite normal limb in each patient. The results were somewhat surprising in that the lowest level of fluorescence in the normal extremity varied in different patients from the ankle to the base of the proximal phalanx. However, wheal fluorescence reached the same level in both the affected and the nonaffected limb in six cases. In only one patient was there a difference in level between the two sides and then it was only 8 cm., the distance between two scratch marks.

The test was then carried out on twenty-eight patients with traumatic aneurysms. In two patients the artery alone was involved and in twenty-six cases there were arteriovenous fistulas. The results are given in Table I. In each case a Matas flushing test was performed at the same time as the fluorescin wheal test. When the lowest level of wheal fluorescence was the same in both the affected and the normal extremity the collateral circulation was interpreted as good. When the lowest level of fluorescence on the affected side did not extend as far distally as that on the normal limb, but if the difference was less than 8 cm., the collateral circulation was termed adequate. In some instances the intensity of fluorescence was equal on both sides at the next to the lowest level, but on the affected side was fainter at the lowest level. Such circulation is considered adequate rather than good (see Fig. 2, *B*). If the difference in level was greater than 8 cm. the collateral circulation was considered to be poor (Fig. 2, *A*).

A. *B.*

Fig. 2.—Types of response with fluorescin wheal test. In *A* the lowest level of wheal fluorescence is just above the mid-calf region on the side of the aneurysm in contrast to *B* in which there is faint fluorescence to the base of the first toe (as on the normal side) although the lowest wheal is fainter than on the control side. The situation in *A* signifies poor collateral circulation, that in *B* is considered adequate. If the lowest level on the affected side equaled that on the control in location and brilliance, the collateral supply would be considered good.

The results of the Matas test agreed fairly well with those of the fluorescin wheal test in regard to operability of the patients. In three cases (Cases 1, 2, and 5) in which the flushing time was more than one minute but less than three minutes, wheal fluorescence indicated adequate collateral circulation. Only one of these patients had a major artery ligated. His collateral supply was found to be perfectly adequate after operation. In one patient (Case 20) the Matas flushing time was just short of three minutes but the fluorescin wheal test demonstrated marked inadequacy of collateral blood flow. This patient subsequently was subjected to lumbar sympathectomy. Unfortunately his collateral circulation was not rechecked following this procedure. However, measurements of the intravascular pressure during the operation[5] indicated

TABLE I. STATUS OF COLLATERAL CIRCULATION PRIOR TO OPERATIONS FOR ANEURYSM

CASE NO.	TYPE OF ANEURYSM	LOCATION	COLLATERAL TIME		COLLATERAL CIRCULATION BY WHEAL FLUORESCENCE	MANAGEMENT OF ARTERY AT OPERATION	REMARKS
			MIN.	SEC.			
1	Arterio-venous	Radial and ulnar	2	20	Adequate	Reconstruction	Ulnar artery remained patent, radial became thrombosed
2	Arterio-venous	Superficial femoral	1	45	Adequate	Reconstruction	
3	Arterio-venous	Popliteal	0	45	Adequate	Reconstruction	
4	Arterio-venous	Popliteal	0	45	Good	Reconstruction	After lumbar sympathectomy
5	Arterial	Superficial femoral	1	30	Adequate	Ligation	Emergency operation because of increase in size
6	Arterio-venous	Popliteal	0	35	Good	Ligation	After lumbar sympathectomy
7	Arterio-venous	Popliteal	0	55	Adequate	Ligation	After lumbar sympathectomy
8	Arterio-venous	Superficial femoral	0	30	Good	Ligation	After lumbar sympathectomy
9	Arterio-venous	Superficial femoral	0	30	Good	Ligation	
10	Arterio-venous	Superficial femoral	0	20	Adequate	Ligation	After lumbar sympathectomy
11	Arterio-venous	Superficial femoral	0	25	Good	Ligation	Very large fistula
12	Arterio-venous	Popliteal	0	50	Good	Ligation	After lumbar sympathectomy
13	Arterio-venous	Superficial femoral	0	50	Good	Ligation	
14	Arterio-venous	Superficial femoral	0	45	Adequate	Reconstruction	
15	Arterio-venous	Popliteal	0	50	Good	Reconstruction	After lumbar sympathectomy
16	Arterio-venous	Femoral popliteal	0	15	Adequate	Thrombosis after reconstruction	After lumbar sympathectomy
17	Arterio-venous	Superficial femoral	0	30	Good	Spontaneous closure	
18	Arterio-venous	Popliteal	0	30	Good	Ligation	Very large fistula
19	Arterio-venous	Superficial femoral	0	30	Adequate	Ligation	Very large fistula
20	Arterio-venous	Popliteal	2	45	Poor	Reconstruction	Measurements of collateral before sympathectomy
21	Arterio-venous	Superficial femoral	0	40	Good	Reconstruction	
22	Arterial	Superficial femoral	0	40	Good	Reconstruction	
23	Arterio-venous	Profunda femoris	0	25	Good	Ligation of branch	
24	Arterio-venous	Medial inferior geniculate	3	30	Poor	Ligation of branch	After lumbar sympathectomy
25	Arterio-venous	Femoro-popliteal	Not obtainable		Poor	Ligation	Large collateral close to aneurysm
26	Arterio-venous	Femoro-popliteal	6	0	Poor	Ligation	Large collateral close to aneurysm
27	Arterio-venous	Superficial femoral	0	55	Good	Reconstruction	After lumbar sympathectomy
28	Arterio-venous	Superficial femoral	3	10	Poor		Large collateral close to aneurysm

that even after sympathectomy the collateral blood supply was inadequate, thereby confirming the results of the fluorescin wheal test.

On twenty-three patients with satisfactory collateral circulation according to the fluorescin wheal test, nine were classified as adequate and fourteen as good. An attempt was made to relate this difference to the Matas flushing time. However, there seemed to be little correlation. Thus, eight of the patients with good collateral supply showed a flushing time of over thirty seconds and only six had an appearance of color in thirty seconds or less. Although six patients in the termed adequate group required over one-half minute for flushing, there were three patients in whom the time for flushing was thirty seconds or less. The fluorescin wheal results seemed to be more in keeping with the clinical impression in the individual case than did the flushing test.

All but one of the twenty-eight patients who were studied have come to operation. The one patient had a spontaneous closure of an arteriovenous fistula while under observation. The artery has remained patent. In two cases the aneurysm was found to originate from a large branch rather than from the main artery: the profunda femoris rather than the superficial femoral and the medial inferior geniculate instead of the popliteal, respectively. Reconstruction of the injured artery was performed successfully in ten cases. Thus, in thirteen cases cure of the aneurysm has been effected without interruption of the major artery.

In the remaining fifteen patients the circulation has been carried on through collateral vessels since ligation of the affected artery was necessary in fourteen patients, and one developed thrombosis of the artery at the site of an attempted repair. None of these patients have developed gangrene and in only two was there transitory coolness and paresthesia of the toes. Preoperative examination, both by wheal fluorescence and by the Matas collateral time indicated adequate or good collateral circulation in twelve cases. Three patients showed inadequate collateral supply by the fluorescin wheal test. The collateral time in two cases was over three minutes, corroborating the results of the fluorescin wheal test. In the third patient an accurate flushing time was not obtainable because of a persistent tendency of the compressor to slip when the limb was moved.

Subsequent observation demonstrated that each of those three patients had an abundant collateral circulation, which was, however, propagated through a vessel that branched off the femoral artery just above or below the aneurysm. Consequently, when the Matas compressor was applied over the aneurysm, it also occluded the chief source of collateral blood flow. In each case the femoral artery was ligated and the aneurysm excised without damaging the collateral branches in the proximity. The postoperative results were satisfactory and one patient had a palpable posterior tibial pulse the day after operation.

The case report of one of these patients is given here to illustrate the method of correlating these special tests for collateral circulation with the other clinical findings.

CASE 26.—A penetrating shell fragment wound of the left thigh, Jan. 20, 1945, resulted in an arteriovenous aneurysm of the femoral vessels just above the adductor canal. The patient was admitted to DeWitt General Hospital three months after injury. The only complaints were aching and swelling of the left leg with prolonged weight-bearing. Examination revealed a small pulsatile mass with a loud characteristic continuous bruit and thrill of arteriovenous aneurysm. The left foot was still somewhat cyanotic and exhibited pallor on elevation. The posterior tibial pulse was markedly reduced in the affected leg. Occlusion of the aneurysm raised the diastolic blood pressure from 50 to 80 and slowed the pulse rate from 100 to 68.

Fig. 3 (Case 26).—Arteriogram. Arrow indicates large branch of femoral artery arising just above the aneurysm. This important source of collateral circulation was cut off by occluding the aneurysm with a Matas compressor.

Despite clinical evidence of a large communication between the artery and the vein, the collateral time was over three minutes and wheal fluorescence did not appear below the level of compressor on the affected leg. A lumbar sympathetic block produced an excellent rise in skin temperature in the left foot but neither test showed improved collateral circulation.

An arteriogram revealed that a large branch of the femoral artery originated just proximal to the aneurysm (see Fig. 3).

This branch, a major source of collateral circulation, was so close to the fistula that it was impossible to occlude the latter by a Matas compressor without obstructing the

branch at the same time. Consequently, both tests of collateral circulation were incorrect since they required a clamp which obliterated an important portion of the collateral blood supply.

At operation the large proximal branch was isolated and preserved above the site of ligation. Postoperative recovery was uneventful and the patient was able to resume moderate activity without evidence of arterial insufficiency.

THE EFFECT OF SYMPATHETIC BLOCK AND SYMPATHECTOMY ON WHEAL FLUORESCENCE

In this series all but two patients had adequate collateral circulation at the time of operation. However, in four cases the fluorescin wheal test indicated inadequate collateral supply at the time of the first observation. A fifth patient seemed to have adequate collaterals according to the level of wheal fluorescence but the Matas flushing time was over three minutes. Two of these patients had a lumbar sympathetic block by the injection of 2 per cent procaine solution into the second lumbar ganglion. While the block was still effective the tests for collateral circulation were repeated. In both cases an improvement in the collateral flow was demonstrated. On the basis of the improved circulation through collateral channels following sympathetic block, lumbar sympathectomy seemed indicated. Not only the two patients tested by procaine sympathetic block but the other three (mentioned previously) with inadequate collateral circulation were also subjected to sympathectomy. The results are given in Table II.

TABLE II. EFFECT OF SYMPATHECTOMY ON COLLATERAL CIRCULATION

CASE NO.	LOCATION	BEFORE SYMPATHECTOMY			AFTER LUMBAR SYMPATHETIC BLOCK			AFTER LUMBAR SYMPATHECTOMY		
		COLLATERAL TIME		COLLATERAL CIRCULATION BY WHEAL FLUORESCENCE	COLLATERAL TIME		COLLATERAL CIRCULATION BY WHEAL FLUORESCENCE	COLLATERAL TIME		COLLATERAL CIRCULATION BY WHEAL FLUORESCENCE
		MIN.	SEC.		MIN.	SEC.		MIN.	SEC.	
4	Popliteal	3	45	Adequate	1	0	Adequate	0	45	Good
6	Popliteal	5	0	Poor				0	35	Good
7	Popliteal	3	15	Poor				0	55	Adequate
8	Superficial femoral	1	45	Poor	0	25	Good	0	30	Good
12	Popliteal	0	40	Adequate				0	50	Good
15	Popliteal	5	0	Poor				0	50	Good
26	Femoro-popliteal	6	0	Poor	5	40	Poor			

It will be noted that four of the five patients were found to have good collateral supply after sympathectomy and the fifth patient was found to have an adequate collateral circulation. The Matas flushing time in each instance was decreased to less than sixty seconds.

Also included in Table II is Case 12 in which there seemed to be adequate collateral supply prior to sympathectomy. The indication for excision of the lumbar ganglia in this instance was the location of the aneurysm low in the popliteal space. Intermittent claudication is frequently severe after arterial ligation at this level even though, as in this case, the collateral circulation

may be sufficient to prevent gangrene. According to the fluorescin wheal test there was a perceptible improvement in the collateral supply after sympathectomy.

In contrast to the effect of lumbar sympathetic block on the criteria of collateral circulation in two patients (Cases 4 and 8), there was no significant improvement in another (Case 26) by either test. This case has been discussed as one of those in which the Matas compressor obstructed a major collateral branch. The effect of sympathetic block was determined before the significance of the large arterial branch was understood and when it was believed that the collateral circulation was actually inadequate. The observation that there was no change in wheal fluorescence after sympathetic block probably saved this patient an unnecessary sympathectomy.

CONCLUSION

The fluorescin wheal test for collateral circulation has been used in twenty-eight cases. Up to the present time it seems to have the following advantages over the Matas flushing time test:

1. Wheal fluorescence provides a clear and definite end point which is not subject to individual variation depending on the person who performs the test.

2. There is no arbitrary time limit. Comparison is generally possible with the opposite normal extremity. The criterion of normal value is provided in the opposite extremity in each observation.

3. Since the extremity does not have to be moved during the test, there is less danger of error from slipping of the compressor.

4. The fluorescin wheal test takes less time than the Matas collateral time technique and, therefore, is less painful to a hypersensitive patient.

Both tests present three defects:

1. Since both procedures require the use of a Matas compressor they are not applicable in cases in which the compressor cannot be used, either because of the anatomic location of the aneurysm (for example, in the subclavian or the iliac vessels) or rarely because the clamp causes severe pain over a sensory nerve involved in scar tissue at the aneurysm site.

2. As in three cases described previously, the compressor may occlude an important collateral branch in the immediate proximity of the aneurysm. This error may be detected by utilizing the information to be obtained from an adequate physical examination and an arteriogram.

3. Although the collateral circulation may be sufficient to prevent gangrene, ligation of a major artery often results in marked limitation of the patient's exercise tolerance because of weakness in an upper extremity or intermittent claudication in a lower limb. Neither test provides any means of anticipating, prior to operation, just how much activity a patient will be able to enjoy after arterial ligation. In general, claudication seemed more severe in those patients whose fluorescin wheal examination suggested adequate collateral circulation than in those patients whose collateral supply was considered good.

SUMMARY

Operative cure of an arteriovenous fistula of a major artery frequently necessitates quadruple ligation of the component arteries and veins. It is necessary to know that the collateral circulation is adequate prior to operation. The Matas-Moszkowicz flushing time test of collateral blood flow has been found to give variable results.

A new method of testing collateral circulation has been devised, based on the observations of Neller and Schmidt on wheal fluorescence. The aneurysm is occluded by a Matas compressor. A series of parallel scratches is made less than 8 cm. apart both on the involved and on the opposite extremity. Ten cubic centimeters of 10 per cent fluorescin are injected into an arm vein and the level of wheal fluorescence is examined by filtered ultraviolet light. If the collateral circulation is adequate, the lowest level of fluorescence should not be more than 8 cm. higher on the involved extremity than on the normal control.

Twenty-eight patients with aneurysms have been examined before operation both by this technique and by the Matas-Moszkowicz test. The fluorescin wheal test seems to give a more accurate picture of the state of the collateral circulation than does the flushing time determination.

REFERENCES

1. Holman, E.: The Immediate and Late Treatment of an Arteriovenous Fistula, Ann. Surg. **122**: 210, 1945.
2. Matas, R.: Testing the Efficiency of the Collateral Circulation as a Preliminary to the Occlusion of the Great Surgical Arteries, J. A. M. A. **63**: 1441, 1914, quoted in Homans, John: Circulatory Diseases of the Extremities, New York, 1939, The Macmillan Company.
3. Neller, J. L., and Schmidt, E. R.: A New Method of Evaluating Peripheral Vascular Diseases, Preliminary Report, Ann. Surg. **121**: 328, 1945.
4. Lewis, Thomas: The Blood Vessels of the Human Skin and Their Responses, London, 1927, Shaw & Sons, Ltd.
5. Freeman, Norman E.: Direct Measurement of Blood Pressure Within Arterial Aneurysms and Arteriovenous Fistulas, SURGERY **21**: 646, 1947.

DIRECT MEASUREMENT OF BLOOD PRESSURE WITHIN ARTERIAL ANEURYSMS AND ARTERIOVENOUS FISTULAS

LIEUTENANT COLONEL NORMAN E. FREEMAN,* MEDICAL CORPS,
ARMY OF THE UNITED STATES
(From the Vascular Surgical Section, DeWitt General Hospital, Auburn, Calif.)

INTRODUCTION

IN THE selection of the optimum time for operation on patients with aneurysms and arteriovenous fistulas, numerous tests for the adequacy of the collateral circulation have been devised. With temporary occlusion of the main arterial supply above the aneurysm, the color and temperature of the skin of the distal parts are noted. The peripheral pulses are palpated or oscillometric readings are made to ascertain the presence of collateral vessels. The Matas-Moszkowicz[1] test which depends upon the reactive hyperemia following temporary total circulatory occlusion is perhaps the most reliable and best known of these tests for determining preoperatively the extent of the collateral circulation. These tests have made operations safe. In the past twelve months eighty-eight patients were operated upon at this Vascular Center with resection of the aneurysms or arteriovenous fistulas without the development of a single case of gangrene of the extremity.

Additional tests have been described which foretell at the time of operation the safety of ligation of the major artery. Observation is made of the temperature and color of the skin of the fingers or toes with temporary compression of the proximal artery. The return flow of blood in the accompanying vein is noted immediately after obstruction of the main artery. Probably the most valid sign is pulsation of the distal artery, the so-called Coenen-Henle phenomenon, even though the main artery is occluded. In the presence of this sign the adequacy of the collateral circulation is probably well established. Various other procedures have been suggested such as making a small incision in the distal part of the extremity or even exposure of a small distal artery to ascertain whether or not there is a supply of blood to the part. All of these tests are useful, but they are qualitative rather than quantitative. Experience in their use is necessary in order to interpret the results. It was felt, therefore, that some more quantitative test for the adequacy of the collateral circulation was needed so that the surgeon at the time of operation could decide whether or not the main arterial supply to the part could be safely ligated.

Direct measurements of the blood pressure within the aneurysmal sac or distal artery appeared to offer a quantitative measurement of the degree of development of collateral circulation. Such measurements have been made in twenty-three cases of arterial aneurysms and arteriovenous fistulas which have come to operation at this Vascular Center in the past six months. By the use

Received for publication, April 30, 1946.

*From the Department of Surgery, University of California Medical School, San Francisco, Calif.

of this technique not only have data been obtained on the development of the collateral circulation, but in addition some facts have been observed in respect to the hemodynamics in these arterial and arteriovenous lesions.

TECHNIQUE

A small, three-way stopcock is fitted with short lengths of rubber tubing connecting a 20 gauge needle with a 10 c.c. syringe. To the third arm is attached an aneroid manometer similar to those used with a blood pressure cuff. The manometer is not sterile, but is enclosed in a sterile transparent oiled silk cover. A diagram of the apparatus is shown in Fig. 1.

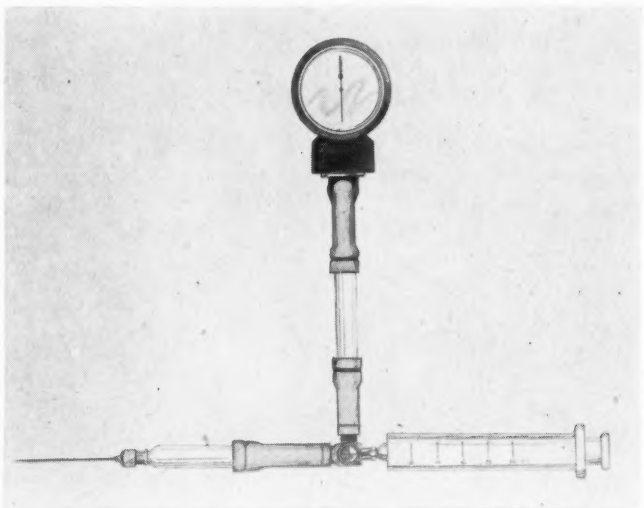


Fig. 1.—Diagram of apparatus used for measuring intravascular pressures in patients with arterial aneurysms and arteriovenous fistulas.*

After operative exposure of the lesion the component vessels are encircled with pieces of rubber tubing or heavy silk thread. The needle is inserted directly into the artery or into the aneurysmal sac and a few cubic centimeters of saline solution are injected in order to clear the system of blood. The pressure can then be read directly on the dial. Oscillations of the manometer needle, although small, indicate the presence of the intravenous needle within the blood stream. After measurement of the initial pressure, the component vessels are temporarily occluded and variations in pressure following each manipulation are noted. After removal of the needle from the artery or sac, only slight temporary bleeding has been observed in the cases.

ARTERIAL ANEURYSMS

Results.—Measurements were made of the intra-aneurysmal pressure in twelve cases of arterial aneurysms. The results are summarized in Table I. In the first patient the collateral circulation had been well established.

Case 3 (Registry No. 4977).—A 27-year-old corporal sustained a rifle bullet injury of the left axilla in 1935 while in civilian life. There were immediate paralysis and numbness

*Illustrations throughout this article are through the courtesy of Museum and Medical Arts Service, U. S. Army Medical Museum.

TABLE I. MEASUREMENTS OF PRESSURES IN ARTERIAL ANEURYSMS

CASE NUMBER	HOSPITAL REGISTRY NUMBER	ARTERY INVOLVED	INITIAL PRESSURE	OCCLUSION OF PROXIMAL ARTERY	OCCLUSION OF DISTAL ARTERY	OCCLUSION OF PROXIMAL AND DISTAL ARTERIES	OCCLUSION OF PROXIMAL AND COLLATERAL ARTERIES	TREATMENT	RESULT
1	6577	Superficial femoral	90*	80				Intrasaccular closure	Ankle pulses present 3 mo.
2	9495	Popliteal	90*	80				Intrasaccular closure	Ankle pulses present 2 mo.
3	4977	Axillary	110	80				Intrasaccular closure	P.O. normal radial pulse
4	8743	Axillary	54	35	60	40		Intrasaccular closure	Circulation adequate
5	7430	Pulsating exophthalmos	110	50			44	Proximal ligation	Slight persistent bruit
6	6643	Axillary	75	60			40	Intrasaccular closure	Circulation adequate
7	8061	Superficial femoral	90	44 54 (2 min.)	94			Transverse repair	Normal circulation
8	8561	Popliteal	74*	(coexistent AV fistula)				Intrasaccular closure	Circulation adequate
9	2898	Axillary	90	32 45 (3½ min.)				Intrasaccular closure	Temporary ischemia
10	3154	Carotid	110	60 84 (30 sec.)				Excision	Hemiplegia after injury
11	4348	Subclavian	86	32	100	18		Intrasaccular closure	Circulation adequate
12	4398	Profunda femoris	34	(thrombus in aneurysm)				Intrasaccular closure	Normal circulation

*Pressure measured before operation by direct puncture.

of the left upper extremity, but function returned about two months after injury. At the time of examination in March, 1945, there was still some residual weakness of the left hand.

He was inducted into the service Dec. 9, 1942, and assigned to an MP battalion. In June, 1944, because of persistent weakness of the left hand, he was admitted to a general hospital and at that time a small pulsating tumor was discovered in the upper part of the left axilla. The radial pulse was found to be weaker on the left than the right side and the blood pressure was 120/90 on the left side and 150/120 on the right side. A systolic murmur was audible over the tumor. While under observation the mass in the axilla increased in size and accordingly he was subjected to operation on May 31, 1945. The third portion of the axillary artery was exposed and a rubber tube was placed about it. The incision was then extended down below the axilla and the brachial artery was exposed. A second piece of rubber tubing was placed about this artery below the aneurysm. Two large collateral arteries were found leaving the axillary artery above the aneurysm and entering the brachial below the sac. After separating the ulnar and median nerve from the surface of the sac, the intra-aneurysmal pressure was measured. In Fig. 2 are illustrated the conditions found at operation.

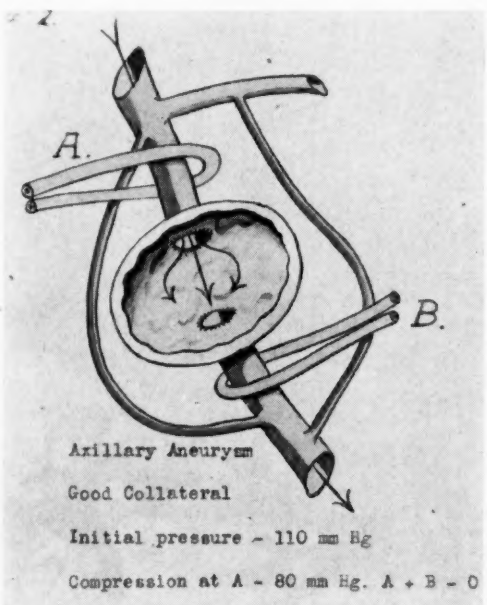


Fig. 2 (Case 3).—Diagram of circulation.

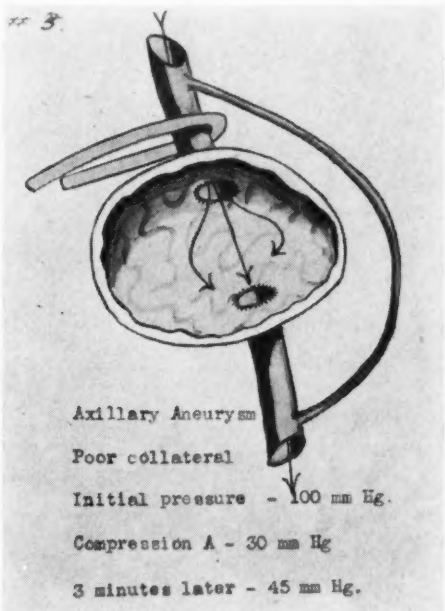


Fig. 3 (Case 9).—Diagram of circulation.

The initial pressure was 110 mm. of mercury. Upon compression of the proximal artery the pressure gradually dropped in 15 seconds to 80 mm. of mercury. The blood was then squeezed out of the sac and the constriction applied as well to the efferent artery. When both the artery leading into and the artery leading out of the sac were occluded, the pressure failed to rise within the sac. The aneurysm was then opened and the arteries leading into it were closed from within the sac. Immediately after operation the radial pulse was palpable on the left side, and the patient made an uninterrupted convalescence. The function of the ulnar and median nerves returned rapidly and he was discharged to duty.

Comment.—Measurement of the intra-aneurysmal pressure in this case was helpful, both in showing that the collateral circulation was well established and in showing that no other vessels communicated with the sac.

The second patient had received the wound more recently and the collateral circulation was poorly established.

CASE 9 (Registry No. 2898).—A 24-year-old sergeant was wounded in the left axilla on June 5, 1944, by a 25-caliber rifle bullet. Because of damage to the brachial plexus he was operated upon Sept. 23, 1944, and a neurolysis of the ulnar, median, and radial nerves was performed. At this time an aneurysm of the axillary artery was noted, but no attempt was made to excise it. Following operation there was improvement in the function of the ulnar and median nerves, but complete paralysis of the radial nerve persisted. Moderate signs of circulatory insufficiency were noted, and attempts were made to improve the collateral circulation by compression of the aneurysm. However, this procedure caused so much pain in the hand that it could not be performed adequately. On July 5, 1945, the axilla was again explored and the third portion of the axillary artery was surrounded by a piece of rubber tubing. A schematic diagram of the component vessels is given in Fig. 3.

Upon constriction of the afferent artery the initial pressure of 100 mm. of mercury dropped to 30 mm. of mercury. The pressure within the aneurysm slowly increased so that 1½ minutes later it was at 40 mm. of mercury and 3½ minutes after constriction of the afferent artery the mean pressure was 45 mm. of mercury. The afferent artery below the aneurysm was likewise secured by a piece of rubber tubing. With both arteries occluded the sac was opened and the component vessels ligated from within the sac. Following this procedure the neurolysis was performed on the nerves of the brachial plexus.

Immediately after operation the hand was found to be cold and cyanotic, but within a period of three hours circulation returned and the patient made a good recovery. The radial pulse was not palpable two months after operation but there were signs of regeneration of the nerves.

Comment.—Determination of the intra-aneurysmal pressure in this case revealed that the collateral circulation was poorly established. The rise from 30 to 45 mm. of mercury in the period of 3½ minutes following occlusion of the axillary artery demonstrated, however, that there were collateral vessels present which could dilate sufficiently to care for the metabolic needs of the tissues of the hand.

In the third patient the collateral circulation was well established, but in addition to the main arteries the patient had some collateral vessels emptying directly into the aneurysmal sac.

CASE 6 (Registry No. 6643).—A 24-year-old sergeant was wounded in the right axilla by a shell fragment on April 9, 1945. He sustained a severe lesion of the brachial plexus and developed a tense, pulsating swelling in the right axilla. He had severe pain and swelling of the hand and forearm. Exploration of the axilla was performed on July 9, 1945, and at that time a large arterial aneurysm was found in the second portion of the axillary artery. After control of the afferent and efferent arteries the pressure within the sac was measured. The initial pressure was found to be 75 mm. of mercury. With compression of the afferent artery the pressure dropped to 60 mm. of mercury. When the efferent artery was also compressed the pressure still remained at 60 mm. of mercury, but upon digital compression of the tissues beneath the sac, it was possible to empty the sac and control the inflow of blood into it. The sac was accordingly opened and two large arteries were found leading into it on the posterior surface. In Fig. 4 is shown the relationship of the collateral arteries to the sac.

These arteries, as well as the openings of the axillary artery, were closed from within the sac. The cords of the brachial plexus were separated from the wall of the sac and the wound was closed. After operation the patient made an excellent recovery, the pain decreased markedly, and some two months after operation there was recovering function of the brachial plexus. At no time was there any evidence of circulatory impairment to the right hand, and the right radial pulse was present after operation.

Comment.—Determinations of pressure in this patient not only disclosed that there was good collateral circulation, but also revealed the presence of the additional arteries communicating with the aneurysmal sac.

The results obtained in the cases of simple arterial aneurysms are summarized in Table I.

In addition to these patients whose pressures were measured at the time of operation, in four additional cases the pressure within the aneurysm was measured by direct puncture through the intact skin before operation. In one patient with an aneurysm of the neck it was demonstrable that the oscillations of the needle could be checked by direct pressure on the common carotid artery at its bifurcation. This patient had developed a hemiplegia immediately following the injury and the demonstration that the pressure within the sac did not drop after occlusion of the common carotid indicated that the internal carotid must have been obliterated at the time of the initial injury. This fact was subsequently borne out at the time of operation.

Fig. 4 (Case 6).—Diagram of circulation.

Fig. 5 (Case 14).—Diagram of circulation.

In a second patient who was suffering from an arterial aneurysm of the superficial femoral artery which had recently started to expand, the pressure within the sac was found to be well maintained after digital occlusion of the superficial femoral artery above the aneurysm. After insertion of the needle he developed severe pain in this thigh, and the ankle pulses, which had previously been present, disappeared. It was felt that thrombosis had occurred within the sac and this fact was confirmed at the time of operation. This patient is the only individual in the series who developed any complication following needling of the aneurysmal sac.

The high initial pressure, 90 mm. of mercury, observed in this patient with a pulsating hematoma which was in the process of expanding accounts for the severe pain, toxicity, and damage to surrounding structures characteristic of such lesions. A similar high pressure was observed in another patient (Case 2) with a pulsating hematoma of the popliteal space. The danger of nerve damage and occlusion of collateral circulation, both arterial and venous, from such unchecked pressure makes early operative intervention necessary.

Simultaneous occurrence of an arterial aneurysm and an arteriovenous fistula has been observed only once at this Vascular Center. The patient (Case 8) sustained a perforating wound of the right popliteal space from a German pistol. He developed marked swelling of the popliteal space and severe ischemia of the leg and foot which resulted in extensive necrosis of the muscles and gangrene of the great toe. The characteristic thrill of an arteriovenous aneurysm was palpable in the popliteal region but in addition a pulsating tumor was also present. Since peripheral gangrene in association with an arteriovenous fistula is exceedingly rare, the possibility of a coexistant arterial aneurysm was considered. Preoperative measurement of the pressure by direct puncture of the aneurysmal sac revealed it to be 74 mm. of mercury, considerably higher than the initial pressure generally found in cases of arteriovenous fistulas. At operation a false aneurysm of the lower popliteal artery was encountered. After intrasaccular closure of the component vessels, an arteriovenous fistula was discovered which involved the artery two inches distal to the first aneurysm. After excision of this fistula adequate circulation was observed.

ARTERIOVENOUS FISTULAS

The pressure was measured within the arteries or aneurysms in eleven patients suffering from arteriovenous fistulas. The results are summarized in Table II. In the first case, in addition to the arteriovenous fistula, there was a large aneurysmal sac in the thigh.

Case 14 (Registry No. 2410).—A 23-year-old sergeant was wounded in the right thigh by a shell fragment on Nov. 21, 1944. Approximately two weeks later a pulsating mass was discovered in the right thigh, and this increased in size for one week. A continuous thrill was palpable over this tumor and on auscultation there was a continuous bruit with systolic accentuation, indicating an arteriovenous aneurysm. An arteriogram, taken Feb. 9, 1945, showed a large aneurysm on the medial side of the right upper thigh with a fistula between the femoral artery and vein. After the collateral circulation had been sufficiently established he was operated upon June 28, 1945. The superficial femoral artery was exposed both above and below the aneurysm and these vessels were controlled by pieces of rubber tubing. A needle was then inserted into the aneurysmal sac and the pressure was found to be 35 mm. of mercury. Upon compression of the artery above the sac the pressure immediately fell to 12 mm. of mercury. Release of the compression allowed the pressure to rise to 35 mm. of mercury. When the distal artery was occluded, the pressure rose to 40 mm. of mercury, indicating that at least some of the blood coming down through the femoral artery was proceeding beyond the fistula into the arteries of the lower leg. In Fig. 5 are indicated the vascular findings.

The femoral artery was then dissected away from the aneurysmal sac and the opening into the latter closed by pressure while the laceration in the femoral artery, which measured 1.5 cm. in length, was closed with a continuous longitudinal suture of 000 black silk

TABLE II. MEASUREMENTS OF PRESSURES IN ARTERIOVENOUS FISTULAS

CASE NUMBER	HOSPITAL REGISTRY NUMBER	ARTERY INVOLVED	INITIAL PRESSURE	OCCLUSION OF PROXIMAL ARTERY	OCCLUSION OF DISTAL ARTERY	OCCLUSION OF PROXIMAL VEIN	OCCLUSION OF DISTAL VEIN	OCCLUSION OF PROXIMAL ARTERY AND BOTH VEINS	TREATMENT	RESULT
13	9416	Superior femoris						72	Excision	
14	4210	Superior femoris	35	12	40				Long repair	Arteriogram P.O.
15	5415	External iliac						54	Excision	
16	4251	Profunda femoris	46	30					Excision	Normal circulation
17	5504	Popliteal	30	22				86	Transverse repair	Arteriogram P.O.
18	4649	Superior femoris	70	10	72	80	70	46	Excision	Slight claudication
19	6842	Popliteal	35	0	30	56	38	10*	Transverse repair	Arteriogram P.O.
20	5876	Superior femoris	30	0	Thrombosed	70	30		Excision	Normal circulation
21	5778	Carotid jugular	30	0	36	64	40	52	Transverse repair	Normal circulation
22	5611	Superior femoris						38	Excision	Normal circulation
23	2819	Common femoris	38	0	48				Excision	Slight claudication

*Additional venous communication discovered after separation of fistula.

on an atraumatic needle. After suture of the artery the rubber tubing was released and good pulsation was transmitted across the suture line. The aneurysm was then opened widely, clots evacuated, and the openings of the femoral vein into and out of the sac were closed with stitch ligatures. No attempt was made to excise the sac. After operation the patient made a good recovery and an arteriogram taken on July 27, 1945, demonstrated patency of the superficial femoral artery.

The second case represents the findings in a simple case of arteriovenous fistula in which the component arteries and veins were readily secured.

CASE 17 (Registry No. 5504).—A 21-year-old soldier was wounded in the right popliteal space by a mortar fragment Dec. 21, 1944. At the time of admission to this Vascular Center on March 28, 1945, he presented typical evidence of an arteriovenous fistula in the popliteal space. An arteriogram taken by injection of diodrast into the femoral artery on May 27, 1945, visualized the femoral artery well to the popliteal space and at this point there was considerable reflux of the opaque material into the popliteal vein. He was operated upon Aug. 9, 1945, and after controlling the circulation through all the component vessels a needle was inserted into the aneurysmal sac and the pressures were measured. The initial pressure was 30 mm. of mercury. With compression of the proximal artery the pressure dropped to 22 mm. of mercury. When the proximal artery and both the component veins were occluded the pressure increased to 86 mm. of mercury, indicating a very abundant collateral circulation. The findings are shown in Fig. 6.

With the vessels controlled the artery was dissected away from the vein and the communication was found to measure 1 cm. in diameter. The opening in the vein was closed with a longitudinal running stitch and the arterial laceration was closed transversely after

excising a wedged-shaped section of the damaged arterial wall. After release of the constricting rubber tubing excellent circulation was observed across the line of suture and an arteriogram taken Aug. 24, 1945, demonstrated the patency of the popliteal artery.

In the third patient there was not only a fistula between the profunda femoris artery and vein with a large aneurysmal sac in the thigh, but in addition the collateral circulation was well developed with considerable supply of blood to the fistula by retrograde flow.

CASE 16 (Registry No. 4251).—A 39-year-old soldier sustained a perforating machine-gun wound of the upper thigh on Sept. 17, 1944, and developed a large arteriovenous aneurysm of the thigh. He was operated upon July 15, 1945, and the common femoral artery was exposed just below Poupart's ligament. A very large profunda femoris vessel was found coming from the posterolateral side of the artery and appeared to communicate with the aneurysm. Compression of this artery, although it reduced the bruit, did not completely abolish it. Dissection was then carried down the thigh to expose the superficial femoral artery at the lower part below the aneurysm. The needle was inserted into the aneurysm and the initial pressure was found to be 46 mm. of mercury. With compression of the profunda the pressure dropped to 30. This failure of the pressure to drop still

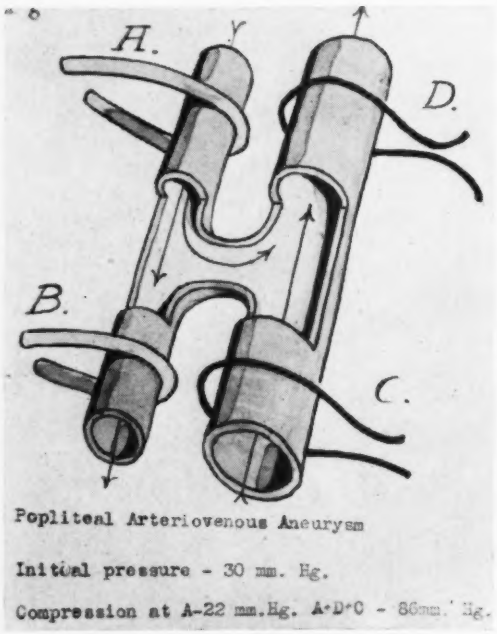


Fig. 6 (Case 17).—Diagram of circulation.

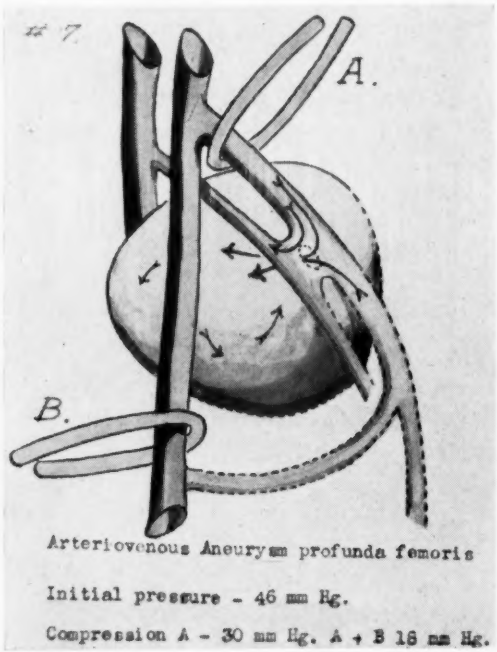


Fig. 7 (Case 16).—Diagram of circulation.

further was interpreted as evidence that considerable collateral supply was entering the sac from below. Constriction of the distal femoral artery now caused the pressure within the sac to fall to 18 mm. of mercury. With the profunda femoris occluded above the aneurysm and the superficial femoral occluded below it, the sac was incised and the openings of the component arteries and veins were controlled by digital pressure until they could be closed with transfixion sutures. Fig. 7 is a diagrammatic drawing of the operative findings. No attempt was made to excise the aneurysmal sac but it was drained through a stab wound on the side of the thigh. The postoperative course was uneventful.

Comment.—Intra-aneurysmal pressure studies in this case were useful in disclosing the presence of large collaterals which had to be secured before the sac could be opened safely.

Arteriovenous fistula between the carotid artery and the cavernous sinus has been observed only once in the series. It was interesting to note the drop in pressure from 110 to 50 with occlusion of the common carotid and a further fall to 44 mm. of mercury when the external carotid was also occluded. Because, in my experience, this pressure was close to the border line of pressure compatible with survival of the peripheral tissues, the external carotid artery was not ligated. Following ligation and division of the common carotid artery this patient had complete cessation of the bruit over the right temporal region for six weeks. A slight recurrence of the bruit was then noted. Exploration of the internal carotid three months later revealed that this artery was thrombosed at the site of the former ligation.

DISCUSSION

The blood pressure levels observed in the cases of arteriovenous fistulas are similar to those reported in the literature. The first reference to this subject was that of Bramann[3] in 1886, who observed a blood pressure varying between 56 and 64 mm. of mercury in a vein of the forearm proximal to an arteriovenous fistula of the brachial vessels. In 1908, von Oppel[4] used a tonometer on the digits and reported in detail the pressures observed in one case of arteriovenous aneurysm of the axillary vessels. The initial pressure was 40 mm. of mercury. With ligation of the proximal artery the pressure dropped to zero. The patient was then returned to the operating theater and the proximal vein was ligated. However, the pressure still remained at zero. Accordingly, the patient was returned to the operating room again and dissection was carried out behind the aneurysm to disclose the presence of a second vein through which the blood escaped from the aneurysm. After ligation of this vein the blood pressure returned to the initial level of 40 mm. of mercury. Korotkow, according to Coenen,[2] used the Riva-Rocci technique for the determination of blood pressure in cases of aneurysms and found that with pressures of 30 mm. of mercury the survival of the peripheral tissues was assured. However, in case the pressure dropped to zero, the outlook was unfavorable. Matas[1] reviewed the various tests and signs which are available for determining the efficiency of the collateral circulation at the time of operation, and commented that he was forced to abandon the blood pressure test even after repeated trials because of the difficulty of obtaining accurate measurements, especially in the lower extremities.

In experimental animals the blood pressure after the production of arteriovenous fistulas has been measured by the use of glass cannulas. Ney[5] in 1913 found in a typical experiment that the arterial pressure decreased from 131 to 80 mm. of mercury. Directly above the fistula the arterial pressure changed from 115 to 83 and the venous pressure increased to 72 mm. of mercury. Although the levels of pressure observed in these experiments are considerably higher than those observed in clinical cases, it is possible that the resistance

offered by the mechanical four-way glass cannulas was greater than that offered by the simple communication between the arteries and veins in these cases.

In studies which were carried on by Reid[6] to investigate the cause for the dilatation of the artery proximal to arteriovenous fistulas, the use of direct measurement of the blood pressure was suggested. The author stated, "Pressures obtained through a needle introduced into the lumen of the vessel seemed plausible and experiments to determine this point are now in progress." Further report on these experiments has not been found.

The dramatic fall of the pressure within the fistula, with ligation of the proximal artery, serves again to emphasize the disastrous consequences which follow this procedure. Matas has repeatedly called attention to the danger of proximal artery ligation and Makins[7] spoke of the high incidence of gangrene observed during the South African war following this procedure. Attention is called to the fact that a very misleading idea of the extent of development of collateral circulation is likely to be obtained from inspection of the distal extremity following temporary occlusion of the proximal artery in cases of arteriovenous fistulas. In one of the patients, after the artery proximal to the aneurysm had been temporarily occluded with a rubber tube, the cadaveric appearance of the foot was so striking that excision of the fistula was deferred, on the basis that the patient did not have adequate collateral circulation. If either or both the component veins or the distal artery had also been occluded at the same time that the proximal artery was obstructed, it is likely that the true character of the collateral circulation would have become evident.

The relatively low pressures observed in aneurysms associated with arteriovenous fistulas is again of significance from the standpoint of the occurrence of secondary hemorrhage. Although the occurrence of expanding hematoma or frank external hemorrhage is not unusual in cases of arterial aneurysms, the occurrence of these complications in arteriovenous fistulas is rare. In a previous communication[8] attention was called to this unusual complication and a case was cited in which the rupture occurred following application of an elastic pressure dressing. Since the pressure within the aneurysmal sac increases abruptly and considerably following obstruction of the venous outflow, as can be seen in Table I, it is not surprising that rupture may be precipitated by the injudicious application of pressure to the tissues surrounding such an aneurysm. Again, thrombophlebitis of the component vein has been observed in three patients at the time of operation for arteriovenous fistulas. It seems possible that occlusion of the venous outflow by thrombophlebitis of the vein might precipitate rupture of an arteriovenous aneurysm, especially if its walls had not become firmly organized.

Pulsating exophthalmos due to a fistula between the internal carotid artery and the cavernous sinus was observed in only one case in this series. It was interesting to note the fall of pressure from 100 to 50 following temporary occlusion of the common carotid artery and a further fall to 44 mm. of mercury when the external carotid artery was also obstructed. It is well known that hemiplegia is more frequent following ligation of the internal carotid artery than it is following that of the common carotid. The observa-

tion here reported offers a quantitative proof of the significance of the collateral circulation maintained through the external carotid artery following obliteration of the common carotid.

No reference has been found to observations on the blood pressure in arteries distal to aneurysms following occlusion of the afferent blood supply. Although the initial arterial pressure in this series was double that observed in the patients with arteriovenous fistulas, the pressure was quite well maintained with one exception following excision of the aneurysmal sac. In this patient the collateral circulation was poorly established. The blood pressure fell immediately from 90 to 32 (see Case 9) and it was only after the patient had been observed for a period of 3½ minutes that the blood pressure increased to 45 mm. of mercury. The gradual rise of pressure over a period of minutes in this patient was probably due to dilation of collateral vessels. The fact that these vessels require time in which to dilate has been utilized in subsequent operations, when complete isolation of the vessels entering the sac has not been feasible. In such cases the main arterial supply has been allowed to remain patent until just before incision of the sac. The proximal and distal arteries have then been abruptly occluded and the sac has been opened immediately. In the short period of time before the collaterals can open widely, the pressure within the arterial system of the extremity is low and visualization of the collaterals emptying into the sac has been facilitated.

The lowest mean arterial pressure observed following excision of aneurysms or arteriovenous fistulas was 32 mm. of mercury. Although no case of gangrene has been observed in this series, in two patients there was evidence of impaired circulation as shown by absent pulses and by intermittent claudication, or increased fatigue following muscular exercise. Although this series is too small upon which to generalize, it may be said that a pressure of 32 mm. of mercury is compatible with an adequate arterial supply to the extremities at rest.

SUMMARY

A method is described for the direct measurement of pressure within arterial aneurysms and arteriovenous fistulas.

The blood pressure within aneurysmal sacs was measured directly at the time of operation in twelve patients with arterial aneurysms and eleven patients with arteriovenous fistulas. The mean initial pressure in the group with the arterial aneurysms averaged 84 mm. of mercury, with variations between 110 and 34 mm. of mercury. Upon constriction of the afferent artery the pressure fell to an average of 58 mm. of mercury. In the patients with arteriovenous fistulas the mean initial pressure averaged 40 mm. of mercury with variations between 70 and 30 mm. of mercury. With constriction of the afferent artery the pressure fell to an average of 10 mm. of mercury.

Determination of the intra-aneurysmal pressure following temporary occlusion of the component vessels has been found to be useful not only in estimation of the degree of development of collateral circulation but also in disclosing the presence of unsuspected collateral vessels which empty into the aneurysmal sac and which must be controlled before the aneurysms can be opened with safety.

The lowest mean arterial pressure found after excision of an aneurysm or arteriovenous fistula was 32 mm. of mercury. With pressures at or above this level, adequate circulation to the peripheral tissues has been observed in these patients.

REFERENCES

1. Matas, R.: Testing the Efficiency of the Collateral Circulation as a Preliminary to the Occlusion of the Great Surgical Arteries, J. A. M. A. **63**: 1441, 1914.
2. Coenen, H.: Zur Indikationsstellung bei der Operation des Aneurysmen und bei den Gefässverletzungen, Zentralbl. f. Chir. **40**: 1913, 1913.
3. Bramann, F.: Das arteillvenöse Aneurysma, Arch. f. klin. Chir. **33**: 1, 1886.
4. von Oppel, W. A.: Zur Operativen Behandlung der Arteriovenösen Aneurysmen, Arch. f. klin. Chir. **86**: 31, 1908.
5. Ney, E.: Ueber die Bedeutung der Venen bei arterio-venösen Aneurysmen, Arch. f. klin. Chir. **100**: 531, 1913.
6. Reid, Mont R.: The Effect of Arterio-venous Fistula Upon the Heart and Blood Vessels, Bull. Johns Hopkins Hosp. **31**: 43, 1920.
7. Makins, George H.: Gunshot Injuries to the Blood Vessels, Bristol, England, 1919, John Wright & Sons, Ltd.
8. Freeman, Norman E.: Secondary Hemorrhage Arising From Gunshot Wounds of the Peripheral Blood Vessels, Ann. Surg. **122**: 631, 1945.

A METHOD OF RAPID TRANSFUSION INTO THE FEMORAL VESSELS IN PATIENTS WITHOUT ADEQUATE PERIPHERAL SUPERFICIAL VEINS

J. Ordie Shaffer, M.D., Minneapolis, Minn.

THE method described here is suggested as an efficient method of rapid transfusion in cases in which the usual venous route is impossible. In many cases of prolonged daily intravenous infusions in which the patient has been on parenteral feedings for weeks the veins of all the extremities are obliterated so that even when multiple venesections are done it is found that the superficial venous channels are unsuitable for infusions. These patients can then, of course, be given hypodermoclysis or proctoclysis if the oral route is not available for feeding, but should an emergency situation such as profound shock arise, plasma or blood is needed urgently and the patient may soon die if the blood volume is not replenished within a short time. The following method of femoral infusions has proved very effective and efficient at the University of Minnesota Hospital in these cases.

After having prepared the skin of the groin adjacent to the inguinal ligament with a suitable antiseptic solution, the area in the groin is palpated for the pulsation of the femoral artery. When a good arterial expansile pulsation is felt, the large common femoral vein just adjacent on the medial side is almost always open and is an excellent site for transfusions. In those cases in which the shock is of such a profound nature that the pulsation of the femoral artery is not perceptible, the adjacent femoral vein is frequently collapsed and a transfusion into the femoral artery is then used. In both cases a two and one-half inch, 20 gauge needle with a short, beveled point is used. In the case of the infusion into the common femoral vein the arterial pulsation is located at or just above the inguinal ligament and the finger tips are arranged in a parallel direction on the medial side of the artery below the inguinal ligament. The needle on a 10 or 20 c.c. syringe is entered through the skin at a point just medial to the artery holding the needle and syringe perpendicular to the surface of the leg. The needle is then slowly advanced until dark venous blood slowly appears in the syringe. The usual range of depth is 2 to 3½ cm. Drawing back the plunger of the syringe is usually not necessary, but may aid in some cases. Following this, 5 to 10 c.c. of blood are withdrawn, injected, and withdrawn to ascertain that the needle is satisfactorily placed within the lumen of the vein. This identical procedure is also used frequently in these cases to draw blood specimens for diagnostic tests. After having carefully determined that the position of the needle is satisfactory or having further inserted or withdrawn the needle 1 or 2 mm. for satisfaction, a small Kelly forceps is clamped (first notch) on the needle as close to the skin line as possible. This is followed by two other forceps, placing each closely on top of the other and placing each approximately 120 degrees away from the other as shown in the accompanying Fig. 1.

Received for publication, April 9, 1946.

The forceps are then taped to the skin and excellent immobilization is obtained in all planes. However, it is usually advised that the patient's leg be restrained if he is comatose or that he be instructed to refrain from gross movements of the leg if he is cooperative. The needle is then disconnected and a glass adapter used to connect the needle to a two-bottle, open intravenous setup so that blood may be pumped in at any rate desired (Fig. 2).

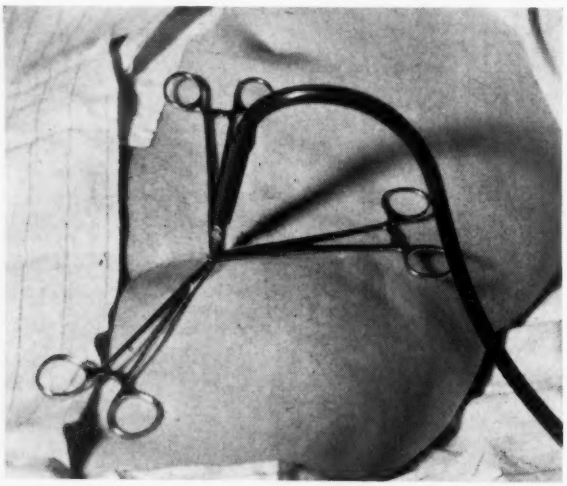


Fig. 1.—Close-up of inguinal region showing method of immobilization of the needle by the application of three forceps.

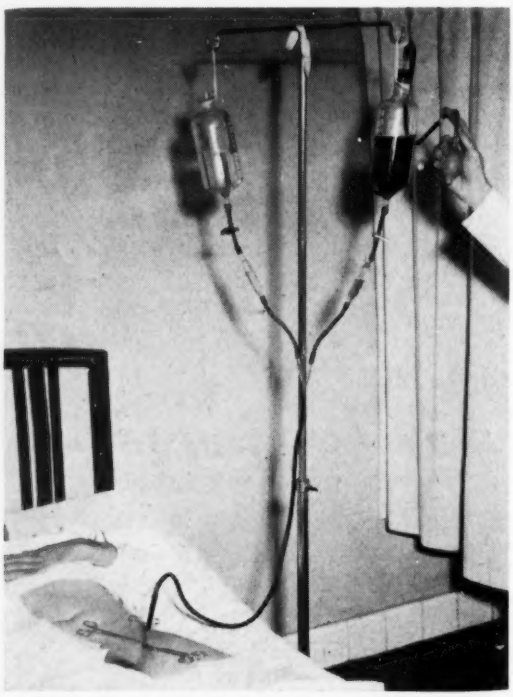


Fig. 2.—Illustration of the entire two-bottle, open infusion setup.

The leg is checked periodically for any swelling adjacent to the needle, but the intraluminal position of the needle can be checked at any time if a translucent solution is being infused by entirely occluding the rubber tubing about one foot from the needle with one hand while the tubing is pinched and released at a point between this level and the needle with position of the needle. This is always followed by an abundant influx of blood back into the glass adapter. In the cases of profound shock in which the femoral artery is used, a technique is used in which the No. 20 needle is inserted in a perpendicular plane at a point midway between the pubic tubercle and the anterior superior spine (point of maximum pulsation, if present) just below the inguinal ligament. A lighter colored blood pulsating rhythmically may force the plunger of the syringe back very rapidly but in cases of profound shock with associated anoxia only a small amount of dark blood may enter the syringe. As the arterial pressure gradually rises, the color of the blood lightens and pulsations increase such that raising the infusion set or increasing the pumping pressure becomes necessary. Simple withdrawal of the needle from the artery or vein and maintenance of pressure for a few seconds has not been followed by a discernible hematoma or concomitant difficulty in any case. The method has been used in five cases of profound shock in which no peripheral superficial veins were available, with gratifying results in each case, such as to encourage further use of the method.

SUMMARY

1. A method of efficient rapid transfusion is presented which is useful in cases in which multiple thrombosis or prolonged trauma to veins make ordinary venoclysis or venesection impossible.

2. The common femoral vein, a site just below the inguinal ligament, is used in those cases in which a good pulsation of the femoral artery is palpable.

3. In those cases in which the shock is of such a profound nature that the artery is not palpable, a concomitant collapse of the femoral vein occurs frequently enough so that the femoral artery is more practicable. The artery is conveniently located at the mid-point between the pubic tubercle and the anterior superior spine.

4. A method of immobilization of the needle is presented.

5. Blood, plasma, or fluids can be dripped or pumped in under pressure at any desirable rate.

6. Simple withdrawal of the needle from the artery or vein and maintenance of the pressure for a few seconds has not been followed by a discernible hematoma or concomitant difficulty in any case.

7. It is hoped that the method may be more widely utilized in emergency situations in patients without an adequate superficial peripheral venous network.

WOUND HEALING STUDIES ON SEVERAL SUBSTANCES RECOMMENDED FOR THE TREATMENT OF BURNS

BROCK E. BRUSH, M.D., CONRAD R. LAM, M.D., AND JOSEPH L. PONKA, M.D.
DETROIT, MICH.
(From the Division of General Surgery of the Henry Ford Hospital)

SEVERAL years ago, a study of the methods of treatment of burns in several large industrial plants revealed that almost a hundred different ointments, powders, and solutions were being used.[1] Almost none of these substances had been subjected to critical investigation with regard to their effect on wound healing. Recently, there has been a trend toward simplification and standardization in local burn therapy. Tannic acid is no longer used and the shortcomings of sulfonamide ointments and many other preparations have been recognized. However, the number of substances which are being advertised and sold as burn remedies is still too large. Several of these which are being used or were formerly used have been chosen for controlled studies. This report also presents the results of tests of some experimental ointments which were undertaken at the request of the Subcommittee on Burns and Surgical Infections of the Committee on Medical Research.

The following substances were tested: tannic acid solution, tannic acid in tragacanth jelly, commercial tannic acid jelly (Amertan), petrolatum gauze, two kinds of carbowax ointment, mineral oil and aluminum monostearate preparation, proflavine dihydrochloride, Biodyne ointment, and Hydrosulphosol solution.

The experimental method was that previously employed by two of us in investigating the effect of a number of agents on the healing of cutaneous wounds.[2] This procedure was essentially that of Carrel and Hartman.[3] Usually, each substance was tested on twelve guinea pigs. Under ether anesthesia, the abdomen was shaved, prepared with an antiseptic solution (hexyl-chloro-m-cresol) and two circular cutaneous defects were made, one being on each side of the midline. The wound on the animal's left was used as the test wound and the other served as a control. The wounds were approximately the same size and were usually about the size of a dime (Fig. 1). The defects were outlined on sterile cellophane to record the size, after which the material to be tested was placed on the appropriate wound. Sterile gauze dressings were placed on each wound and held with adhesive tape which passed entirely around the animal's body. The dressings were changed every two days until both wounds were healed. At each dressing, tracings of the wound areas were made and more of the test substance was applied. The cellophane tracings were transferred to white paper for a permanent record (Fig. 2).

Part of the work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Henry Ford Hospital.

Received for publication, June 26, 1946.

A typical experiment on twelve animals is represented by the results obtained by the application of 5 per cent tannic acid solution (Table I). It is seen that in no instance did the wound treated with the test solution do better than the control, and in eight of the ten animals who survived, there was delay in healing of the treated side. From this, it is concluded that the solution is inhibitory to wound healing and in the summary column in Table III, this effect is indicated.

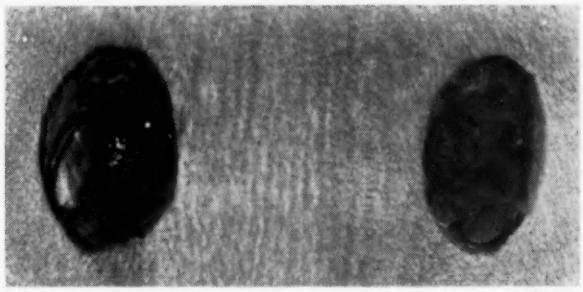


Fig. 1.—Freshly made cutout wounds on the abdominal wall of the guinea pig; the experimental substance will be applied to the wound on the animal's left.

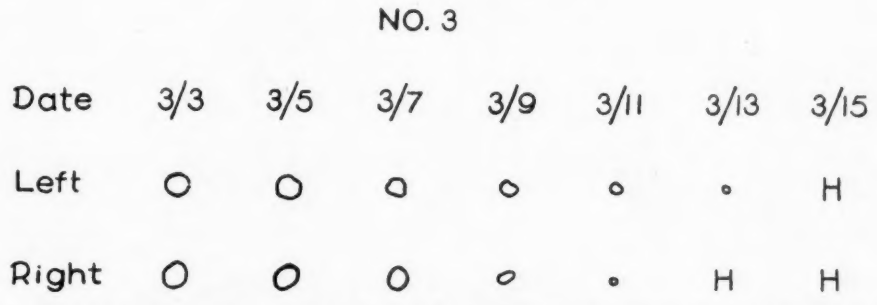


Fig. 2.—Tracings showing rate of healing in a typical experiment; hydrosulphosol was applied to the wound on the left at each dressing. Note that the control wound healed first.

A second typical experiment is illustrated in Table II. In eight, or two-thirds, of the animals treated by the application of hydrosulphosol solution, at least one more dressing was necessary on the treated side and it is concluded that the material is moderately inhibitory.

COMMENT ON THE SUBSTANCES TESTED

Since the use of tannic acid in burns has fallen into disrepute because of the toxic effect on the liver and the demonstration by several investigators that there is inhibition of wound healing,[4-6] it might seem unnecessary to give this method further consideration. Actually, however, the experiments on tannic acid in tragacanth jelly were carried out in May, 1941, at a time when the coagulation method of treatment was being used extensively. The subsequent tests were made to confirm the growing suspicion regarding tannic acid and to show the value of this simple pilot type of experiment. Since twenty-five of the twenty-eight treated wounds showed delay in healing, it is impossible to escape

the conclusion that tannic acid is detrimental to wounds. If this experiment had been done years ago, it probably would have led to an earlier careful scrutiny of the tanning method (Fig. 3).

Petrolatum gauze has been used extensively as a dressing for burns, granulating surfaces, and skin graft donor sites. It has been generally assumed that it is an inert type of dressing. Often, it is spoken of as a control treatment as compared with a presumably active substance. In these experiments, petrolatum

TABLE I. FIVE PER CENT TANNIC ACID SOLUTION
(DAYS REQUIRED FOR HEALING)

ANIMAL NUMBER	CONTROL WOUND (DAYS)	TEST WOUND (DAYS)	HEALING
1	15	19	Delayed
2	Expired third day		--------
3	13	23	Delayed
4	11	19	Delayed
5	15	21	Delayed
6	19	21	Delayed
7	13	15	Delayed
8	15	21	Delayed
9	11	11	No effect
10	11	21	Delayed
11	15	15	No effect
12	Died eighth day		

Summary: Delay in eight of ten animals which survived; cause of death in two animals not known.

TABLE II. HYDROSULPHOSOL SOLUTION
(DAYS REQUIRED FOR HEALING)

ANIMAL NUMBER	CONTROL WOUND (DAYS)	TEST WOUND (DAYS)	HEALING
1	10	14	Delayed
2	10	12	Delayed
3	10	12	Delayed
4	12	12	No effect
5	10	12	Delayed
6	12	12	No effect
7	12	14	Delayed
8	10	12	Delayed
9	12	12	No effect
10	8	10	Delayed
11	10	12	Delayed
12	12	12	No effect

Summary: Delay in wound healing in eight of twelve animals.

TABLE III. SHOWING NUMBER OF ANIMALS IN WHICH HEALING WAS HASTENED, UNAFFECTED, OR DELAYED, WITH CONCLUSIONS AS TO EFFECT OF TEST SUBSTANCE

SUBSTANCE TESTED	HASTENED	NO EFFECT	DELAYED	CONCLUSIONS
Tannic acid solution (5% aqueous)	0	2	8	Delayed
Tannic acid jelly (tragacanth)	0	0	6	Delayed
Tannic acid jelly (Amertan)	0	1	11	Delayed
Petrolatum gauze	3	7	2	No effect
Carbowax ointment A	2	4	6	Delayed (?)
Carbowax ointment B	1	5	5	Delayed (?)
Stearate grease	2	5	2	No effect
Proflavine dihydrochloride	0	5	7	Delayed
Hydrosulphosol solution	0	4	8	Delayed
Biodyne ointment	2	4	6	Delayed (?)

gauze was compared with a dry gauze dressing. It appeared to have no effect on the time necessary for the healing of these small wounds.

During World War II, the Subcommittee on Burns and Surgical Infections of the Committee on Medical Research interested itself in a search for better ointment bases to be used as vehicles for the sulfonamides and penicillin and for use as bland dressings or for gauze impregnation. At the request of the committee, we carried out some tests on a carbowax base in two combinations. That referred to in Table III as carbowax A had the following composition: carbowax* 4000, 21 Gm.; propylene glycol,* 64.5 Gm.; methyl cellulose (25 c.p.s) 2.5 Gm.; Vodol O.F. (lecithin) 0.25 Gm.; and mineral oil, 12 c.c. To this mixture was added 12 per cent of a lipophilic base consisting of aluminum monostearate-mineral oil base containing Tween 60.

Each type of carbowax ointment tested showed slight delay in wound healing in one-half of the animals.

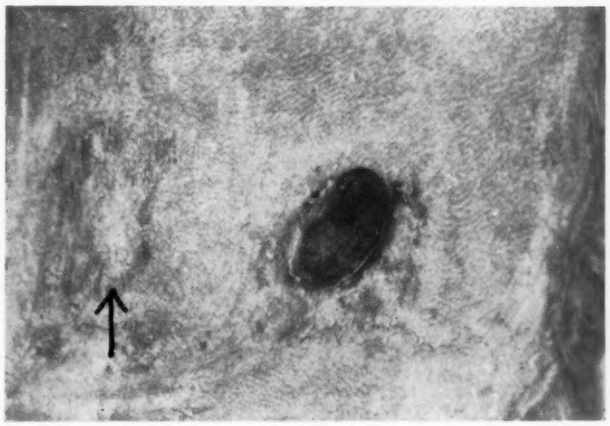


Fig. 3.—Delay in healing from the use of tannic acid jelly; the control wound, on the animal's right, is healed.

Another experimental ointment which was studied was that referred to in Table III as stearate grease. This was a mixture of mineral oil and aluminum monostearate. The wounds dressed with this healed in the same time as the controls. In a series of twelve animals, stearate grease was applied to one wound and carbowax A to the other. In one-half of these, the side with stearate grease healed first, in four the rate of healing was the same, and in two the side with carbowax healed first, indicating a slight advantage for the grease.

During the war, there was a revival of interest in a group of local antiseptics known as animoacridine compounds or flavines. This was particularly true in Great Britain. One group[7] advised the use of proflavine sulfate for granulating areas and burns. Other investigators[8] showed that a 1:1000 solution of proflavine buffered to a pH of 6.2 was harmless when applied to the rabbit's exposed

*The carbowax and propylene glycol were obtained by the committee from the Union Carbide and Carbon Company. Carbowax B was an ointment prepared by the Rystan Company and was said to consist of carbowax 4000, carbowax 1500, glyceryl monostearate, propylene glycol, and distilled water.

brain tissue. (In the same experiment, acriflavine in that concentration produced tissue damage.) Proflavine dihydrochloride* was applied to the test wound in twelve of our animals. The control wound healed first in seven animals, indicating a slightly inhibitory effect of the test solution.

From time to time, there has been interest in the role of sulfur in wound healing. In 1930, Reimann published a paper entitled "Use and Reasons for the Use of Thiocresol to Stimulate Wound Healing."[9] In this article he stated, "The naturally occurring chemical radical -SH which stimulates mitosis has been discovered. Advantage is taken of the chemical group sulphydryl to stimulate the healing of wounds." It is notable that neither of the two wounds described in the communication were entirely healed at the time of the report. Further favorable comment followed.[10] Then there were several papers[11-13] recommending the use of a proprietary preparation, hydrosulphosol, which contains the –SH radical (sulphydryl). A critical review of these three papers leaves one unconvinced that the solution actually had a beneficial effect on the burns. Tissue culture studies by Salle and Korzenovsky[14] showed that chicken heart cultures in contact with the material failed to grow unless the hydrosulphosol was diluted 1:80. With seventy-two hours contact, it was necessary for the dilution to be increased to 1:400 before there was growth of the culture.

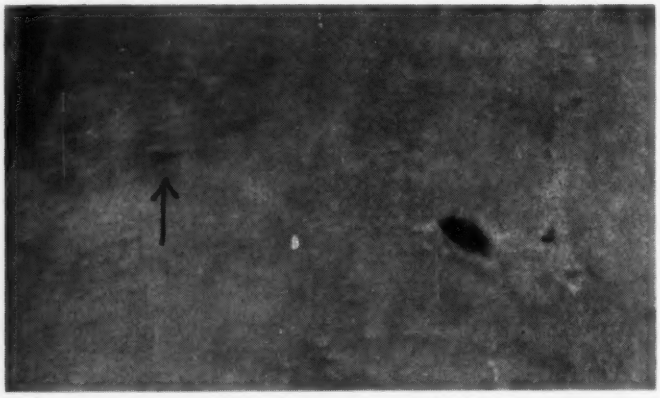


Fig. 4.—Delay in wound healing with the use of hydrosulphosol; the control wound (arrow) is healed.

When hydrosulphosol was tested on the guinea pig wounds, there was delay in healing in two-thirds of the animals (Table II and Fig. 4). In no instance did the treated side heal before the control side. The conclusion was that the material was moderately inhibitory to wound healing.

About three years ago, several lay publications contained some accounts of a preparation known as biodyne ointment, and it was alleged that there was remarkable rapidity of healing when the substance was applied to burns.[15, 16] Shortly afterward, Hirshfeld, Pilling, and Maun[17] tested biodyne on dermatome graft donor sites on human beings and experimental animals. The control wounds were covered with petrolatum gauze. They found no evidence that

*Manufactured by Mallinckrodt Chemical Works, St. Louis, Mo.

biodyne accelerated the healing process. Current advertising states that the ointment embodies the property of "acceleration of rate of healing and epithelization."

In our experiments, the control wound was healed before the wound treated with biodyne in one-half of the series. Twice the treated wound healed first; in the remaining four animals both wounds healed on the same day.

SUMMARY

A number of substances which have been suggested or recommended for the treatment of burns have been applied locally to small wounds in guinea pigs and the healing time compared with that of control wounds in the same animal which were treated with dry gauze. Tannic acid in solution and in jellies caused a marked delay in healing. Proflavine dihydrochloride (1:1000) and hydrosulphosol were moderately inhibitory. Biodyne ointment and two kinds of carbowax base gave slight delay in one-half the animals. Wounds dressed with petrolatum gauze and a stearate grease healed in the same time as the controls.

REFERENCES

1. McClure, Roy D., and Lam, C. R.: A Statistical Study of Minor Industrial Burns, J. A. M. A. **122**: 909, 1943.
2. Brush, B. E., and Lam, C. R.: The Effect of the Topical Application of Several Substances on the Healing of Experimental Cutaneous Wounds, SURGERY **12**: 355, 1942.
3. Carrel, A., and Hartman, Alice J.: Cicatrization of Wounds: I. The Relation Between the Size of the Wound and the Rate of Its Cicatrization, J. Exper. Med. **24**: 429, 1916.
4. McClure, Roy D., Lam, C. R., and Romence, Harvard: Tannic Acid and the Treatment of Burns: An Obsequy, Ann. Surg. **120**: 387, 1944.
5. Cannon, Bradford, and Cope, Oliver: Rate of Epithelial Regeneration: A Clinical Method of Measurement and the Effect of Various Agents Recommended for the Treatment of Burns, Ann. Surg. **117**: 85, 1943.
6. Hirshfeld, J. W., Pilling, M. A., and Maun, M. E.: A Comparison of the Effects of Tanning Agents and of Vaselined Gauze on Fresh Wounds of Man, Surg., Gynec. & Obst. **76**: 556, 1943.
7. Heggie, R. M., Gerrard, E. A., and Heggie, J. F.: Superficial Granulating Areas Treated With Antiseptic Emulsions, Lancet **1**: 347, 1942.
8. Russell, Dorothy S., and Falconer, M. A.: Antiseptics in Brain Wounds: An Experimental Study of the Histological Reaction of Cerebral Tissues to Various Antiseptic Solutions, Brit. J. Surg. **28**: 472, 1941.
9. Reimann, S. P.: Use and Reasons for the Use of Thiocresol to Stimulate Wound Healing, J. A. M. A. **94**: 1368, 1930.
10. Birnbaum, I. R.: Thiocresol in Wound Healing and in Skin Grafting, Ann. Surg. **96**: 467, 1932.
11. Pierce, W. F.: The Use of a Sulphydryl Solution in the Treatment of Burns, Am. J. Surg. **53**: 434, 1941.
12. Cruthirds, A. E.: The Treatment of Face and Eye Burns: With a Sulphydryl Solution, Indust. Med. **11**: 109, 1942.
13. Mellon, R. R.: A New Sulphydryl Solution: for the Treatment of Burns, Indust. Med. **11**: 14, 1942.
14. Salle, A. J., and Korzenovsky, M.: Nature of Hydrosulphosol and Its Toxicity to Living Embryonic Tissue, Proc. Soc. Exper. Biol. & Med. **49**: 212, 1942.
15. Time Magazine **40**: 94, 1942.
16. Reader's Digest **42**: 75, 1943.
17. Hirshfeld, J. W., Pilling, M. A., and Maun, M. E.: The Use of Bio-dyne Ointment for Burns, J. A. M. A. **123**: 476, 1943.

THE TREATMENT OF BEDSORES IN PARAPLEGIC PATIENTS

MAJOR BROMLEY S. FREEMAN, MEDICAL CORPS, ARMY OF THE UNITED STATES

(From the Section on Plastic Surgery of the Hines Memorial Hospital, Hines, Ill.)

UNTIL very recently the active surgical treatment of bedsores, especially those in paralyzed patients, not only has been neglected but condemned. Munro[1] in an excellent résumé of the care of spinal cord injuries published in 1940 advised against any form of surgical interference. The literature is replete with injunctions regarding the prevention of bedsores, with multiple recipes for salves, ointments, and local applications; a myriad of beds including sawdust, water, air mattress, as well as plaster casts, frames, and suspension apparatus have been advocated. Except for Davis[2] who advised the replacement of atrophic scars resulting from bedsores by means of plastic procedures thus giving padding to bony prominences, no advocate for the surgical treatment of the ulcerated lesion had come forth until reports of the treatment of paraplegic patients in World War II were announced.[3-5]

As one of the centers for treatment of spinal cord injuries requiring the group consultation of neurosurgeon, urologist, physical therapist, orthopedist and plastic surgeon, we were confronted with approximately 200 ulcers in approximately fifty patients. Traditional passive therapy was continued until, in an otherwise healthy patient, a large ulcer exposing the entire sacrum caused a secondary osteomyelitis and finally a *Bacillus proteus* septicemia. Although massive penicillin therapy was instituted immediately and surgical attempts to control the infection were made, the patient died. At this point a critical survey of the spontaneous healing and the results of our passive treatment pointed to the necessity for a more dynamic approach.

Lewis[6] has shown that ischemia of six to twelve hours damages the skin; continuous ischemia for twenty-four to forty-eight hours or frequently shorter periods results in necrosis of the skin. Relief of ischemia, if not prolonged, is followed by a reactive hyperemia which flushes out the injurious metabolites and restores the tissue if the relief interval is long enough. Moreover, Lewis and others have shown that in normal individuals a pressure of 50 to 60 mm. of mercury is sufficient to arrest the blood flow to the skin. In the normal individual muscular tone and firm subcutaneous tissue interpose a padding between the arterial supply and the pressure points, permitting a more diffuse spread of pressure. Removal of these interposing factors would permit a viselike obliteration of the vessels between the skeleton and the point of pressure. Lessening of the padding between the nonresistent hard surface and the bony prominence through disuse atrophy, as well as by alteration of the skin and tissues by hypoproteinemia, causes a tighter tourniquet around an area of skin, augments the

This article has been released for publication by the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration. The opinions and views set forth are those of the writer and are not to be construed as reflecting the policy of the Administration.

Received for publication, June 24, 1946.

constricting pressure, and obliterates the local circulation. In paraplegic patients lessening of the padding between the skin and the bone, not only by disuse atrophy but through the loss of subcutaneous fat due to general debility, alteration of the elasticity of the tissue by absence of muscular tone, and hypoproteinemic edema, reduces the normal buffering effect, and pressure is placed directly upon the local blood vessels permitting arrest of the blood flow and ischemia. Moreover, the disuse of the legs and hips results in a decreased blood supply to this area, resulting in atrophy of tissue and an obvious impairment in healing.

Experimentally, however, local reflex tests of the circulation on all of our patients showed good results with histamine and scratch. Compared with normal skin above the line of the cord lesion the lower extremities showed an equal timed response to the histamine flare and wheel as well as the tache test, giving evidence of good local circulation. Except for the reduction of the blood supply and the anesthesia in these paralyzed individuals, we found no contraindications for operating other than those found in sympathectomized limbs. In the treatment of severely injured extremities and in postirradiation defects, we had noted the improved circulation developed by rotating, tubed, or pedicle flaps and felt that, with a minimum of trauma, surgical closure of these defects could be carried out.

Clinically, three types of onset of the decubitus ulcers have been noted in the group of patients under study. The first and most common after slight trauma in well-nourished individuals showed a purplish discoloration of the skin followed by swelling, a gradual change in color to normal, and later a small central necrotic area. A second type usually seen after prolonged trauma in well-nourished individuals had its onset in vesiculation followed by epidermal necrosis, leaving nonhealing, shallow ulcerations with piled up hyperkeratotic borders, which showed no change for periods of months. The third type found in debilitated patients showed immediate blanching, followed by massive necrosis and slough invading deeply into the tissue spaces. Repeated insult or infection will permit the formation of the usual extensive, undermining advancing ulcer.

The majority of patients received their initial bedsores in some period before or during evacuation while they lay for hours without turning. However, despite the most exacting nursing care we have observed bedsores arise almost spontaneously in patients who are debilitated markedly and show a depleted protein level. Unless their protein level is kept very high, the slightest trauma, overmassage, or too intensive local heliotherapy can result in ulceration. The average patient under our care had lost from 20 to 30 pounds, had no appetite, and their already depleted protein reserves were gradually draining from ulcerations. As anorexia was common and high protein, high caloric diets of little value unless they were ingested, recourse was made to intravenous protein hydrolysates, plasma, and blood as well as interval oral amino acids. As shown by Mulholland,[7] many ulcers healed spontaneously and most of them diminished markedly in size as soon as the negative nitrogen balance was compensated. Extra vitamins were given with emphasis on vitamins B and C,

and the time-honored preprandial insulin, 5 to 10 units, was given to those with intractable anorexia resulting in a rather marked improvement in appetite and a consequent rise in body weight and serum protein. As the blood supply of the surrounding area appeared inadequate for the disposal of dead tissue, all sloughs were removed surgically. Local dressings of tyrothricin on fine mesh gauze were allowed to dry in place and mechanic's waste used for pressure dressings. Many of the ulcers, especially those around the groin, were exposed to the air for prolonged periods to permit drying. At no time were continuous wet dressings, which macerate the skin, or ointments used. The tendency of the ulcers to undermine and form deep extensive sacculations between tissue spaces was most frequent over the sacrum and trochanters. In several cases the lining of the sac was attached to the periosteum and almost completely encircled the bone. These were mechanically cleaned with irrigations of hydrogen peroxide and saline and packed with tyrothricin-impregnated fine mesh gauze. It was found impracticable to attempt sterilization of the ulcer, and clinical evidences of clean margins and absence of signs of inflammation were used to determine the appropriate time for surgery. Nonetheless, bacteriologic studies of many of the ulcers were made to be certain that any specific therapy could be instituted at once. Elevated temperature, urinary sepsis, and gross infection were the only contraindications to operation. Emaciated patients were prepared by multiple transfusions, plasma infusions, and other intravenous medications. These patients despite a very high protein intake showed evidence of a negative nitrogen balance because of the marked loss through drainage from the dressings, and it was thought advisable to institute surgery as soon as feasible.

The choice of the type of surgical intervention was dependent upon the individual case. Split-thickness skin grafts (.012 to .018 inch) were used to cover extensive sacral ulcers draining large amounts of protein in debilitated patients as a temporary expedient. Skin grafts were also used to close superficial epidermal necroses over well-padded areas. Several hyperkeratotic lesions on the buttock were similarly excised and grafted.

Penetrating ulcers forming saclike projections vastly larger than the external orifice were carefully dissected en bloc. The excision was carried out by sharp dissection without entering into the grossly contaminated sac. Any break in technique called for discarding the contaminated instrument or glove. In several cases the bare bone was exposed and every attempt was made to remove the sac lining completely, though the temptation was very great to curette the surface and leave the bone covering intact. Although microscopic examinations of the lining revealed epithelialization for only a few centimeters or less directly under the external opening, it was felt that the blood supply was insufficient to cope with even the slightest amount of contaminated tissue left behind, and the entire scar tissue was removed.

The closure of the external defect was dependent upon the position of the lesion, the laxity of the tissue, and the presence of other bedsores. Direct primary approximation was carried out only when layers of fascia could easily be brought together to take tension off the skin and wide undermining permitted easy closure without tension. This was possible only in lesions of the anterior-

superior spine area and the small but deeply invasive gluteal ulcers. Larger gluteal ulcerations and smaller trochanteric lesions were closed by advancement flaps or swinging flaps with marked undermining and careful approximation of the subcutaneous layers. Thick rotation flaps either singly or double were used for closure of the larger defects over the trochanters, the sacrum, and the ischial spines. Marked undermining usually lessened the original defect and in the majority of cases the donor site could be closed by primary suture. However, when any evidence of tension presented, the donor site was closed with a thick split-thickness graft.

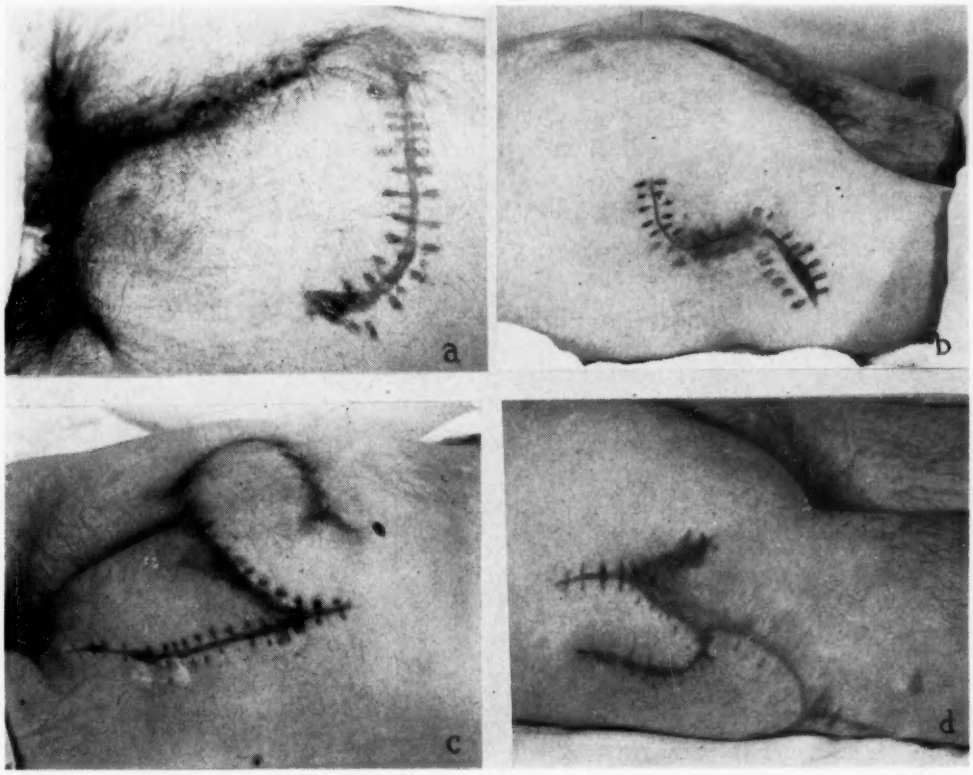


Fig. 1.—Types of repairs after excision of scar, ulcer, and deep extensions. *a*, Defect (5 by 7 cm.) of right gluteal region repaired by wide undermining and simple advancement flap. *b*, Two rotation flaps in form of Z plasty used to close defect after excision of trochanteric ulcer with adherent periosteal extension (shown in Fig. 2). *c*, Transposition flap from right gluteal region closing 8 by 10 cm. sacral defect. *d*, Extensive trochanteric lesion closed by rotation flaps from thigh and gluteal region.

Technically, meticulous care was used in handling the flaps to avoid undue trauma. Fine tissue hooks were used throughout; mosquito clamps and hot packs were used for hemostasis and only the finest cotton sutures for ties and closure. In the earlier cases sulfadiazine was dusted into the wound, but later a solution of penicillin was instilled after hemostasis was completed, the wound irrigated, and the sutures ready for tying. After a few seromas in the larger wounds it became a practice to insert a thin half-tube drain through a stab wound to aid the removal of serum and blood upon the application of a large pressure

dressing of mechanic's waste held in place by elastoplast adhesive or elastic bandage. This drain was removed in twenty-four hours. Replacement of blood loss was carried out by transfusion during or immediately after the operation. Penicillin was administered twenty-four hours prior to the operation and continued systematically for seven to ten days when the sutures were removed and collodion or adhesive bridges used to support the edges. Turning was carried out at three-hour intervals but the operative sites, although well padded with mechanic's waste pressure dressings, were spared. As shown by the examples in Fig. 1, allowing the skin sutures to remain for any period over a week resulted in crosshatching and scarring. Nonetheless, because of the tendency toward delayed tissue repair and the possibility of wound separation, it was thought advisable to forego cosmetic perfection and tend toward a stable wound.

Fig. 2.—Trochanteric ulcer with periosteal extension dissected out en bloc. Note small external opening and large deep extension which surrounded the greater trochanter (see Fig. 1, *b*).

Immediately after hearing of the excellent work of Gibbon and Freeman,[8] a few multiple rotating flap operations entailing a dissection of the entire lumbar sacral and upper gluteal region were done, but the vast extent of the dissection and the blood loss in already debilitated patients persuaded us to return to single rotating flaps. Croce's[9] operation, similar in extent, also entails a midline scar directly over the lumbar and sacral spines which it is felt will be subject to later trauma. In some of the better nourished patients who have thin adherent scars, excision of the sacral and trochanteric areas have been carried out and flaps used for replacement as suggested by Davis.[2] After fourteen days light massage was given under the direct supervision of the surgeon to loosen the wound, mobilize the scar, and increase the local nutrition. At no time was heliotherapy administered locally.

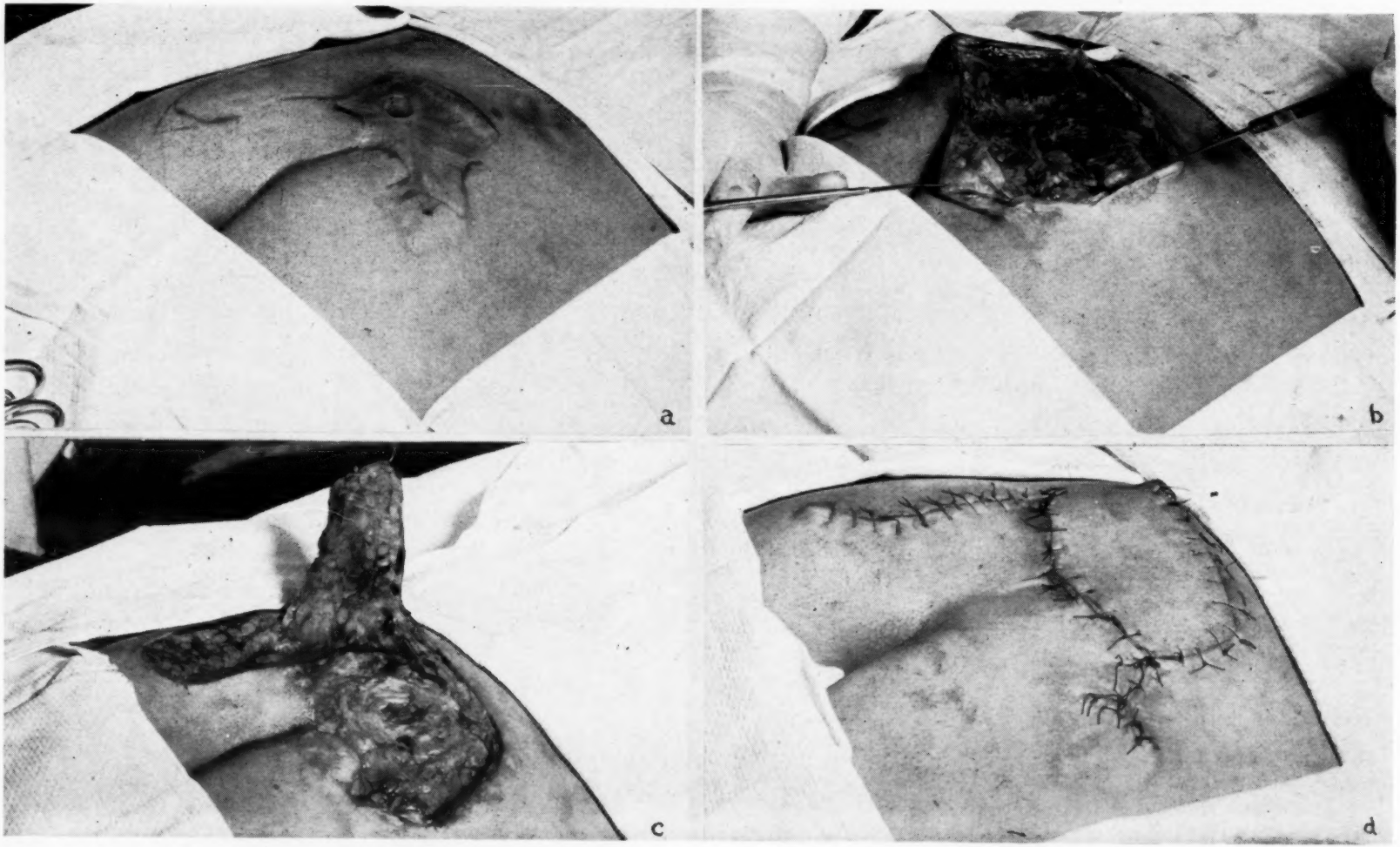


Fig. 3.—Rotation flap method of closing sacral defect. *a*, Improvement in patient's nutrition sufficient to permit partial scar closure of sacral ulcer; deep extension is not visualized in photograph. *b*, En bloc excision of scar, ulcer, and extension down to sacral periosteum in midline. *c*, Left gluteal flap raised and adjacent area undermined at fascial level. *d*, Flap transposed and defects closed; sufficient laxity resulted from undermining to permit right-sided plastic closure.

In only three out of fifty cases were there recurrences of bedsores. Two patients with well-healed flaps over the ischial tuberosities insisted upon sitting through dinner and a long show lasting eight hours with resultant ulcerations directly over the flap. A third patient with a healed thick skin graft over the sacrum blatantly refused either to eat or to get off his back. The constant pressure, plus urinary sepsis, permitted the skin graft to vanish in less than two weeks. A review of these three patients revealed that in the first two the protein levels, although high after preliminary treatment, had been allowed to fall from 8 and 7.6 mg., respectively, to 6.3 and 5.7 milligrams. The third patient's protein level had never gone above 5.8 mg. and was definitely on the downgrade. A checkup on the rest of the operative patients showed an increase in protein level rather than a decrease, and, although several others had attended the dinner and a show for so prolonged a period, only those two with a diminished protein level had a recurrence. The operative procedures are prolonged and tedious, but the results obtained, the improvement of general health, and the restoration of ambulation in wheel chair, crutches, or braces, as well as the frequent discharge of these patients to their homes without the need of constant dressings and drainage, have paid dividends. We no longer watch, over a period of six months or a year, for the slow spontaneous healing of ulcers which result in tissue-paper thin scars easily traumatized.

The youth and excellent health of the patients prior to injury have tremendously influenced our results, but a dynamic approach to the problem of bedsores even in the aged should show returns in longevity and general improvement. It must be emphasized, however, that this regime could not have been carried out without the cooperation of an interested and aggressive urologist[10] and an indefatigable staff of nurses and dietiticians.

SUMMARY

A review of 200 bedsores in fifty paraplegic patients revealed that simple operative procedures could be carried out successfully to close the defects if plasma protein levels were raised to and maintained at normal.

REFERENCES

1. Munro, D.: Care of Back Following Spinal Cord Injuries, New England J. Med. **223**: 391-398, 1940.
2. Davis, J. S.: Operative Treatment of Scars Following Bedsores, SURGERY **3**: 1-8, 1938.
3. Lamon, J. D., Jr., and Alexander, E., Jr.: Secondary Closure of Decubitus Ulcers With Aid of Penicillin, J. A. M. A. **127**: 396, 1945.
4. Barker, D. E.: War Wounds of Spinal Cord; Surgical Treatment of Decubitus Ulcers, J. A. M. A. **129**: 160, 1945.
5. Cutler, C. W.: Discussion of Barker.[4]
6. Lewis, Thomas: Vascular Disorders of the Limbs, New York, 1936, The Macmillan Company, p. 97.
7. Mulholland, J. H., and others: Protein Metabolism and Bed Sores, Ann. Surg. **118**: 1015-1023, 1943.
8. Gibbon, J. H., and Freeman, L. W.: Surgical Conference of the Sixth Service Command, July, 1945.
9. Croce, E. J., Schullinger, R. N., and Shearer, T. P.: Operative Treatment of Decubitus Ulcers, Ann. Surg. **123**: 53, 1945.
10. Baumrucker, G.: Management of Paralyzed Bladders of World War II Casualties, J. Urol. (In press.)

ACUTE CHOLECYSTITIS

With Special Reference to the Occurrence of Jaundice

L. J. Lester, M.D., New York, N. Y.

(From the Surgical Service of Dr. Ralph Colp, The Mount Sinai Hospital)

INFLAMMATION of the gall bladder is one of the most common of disease entities, and because of its frequent occurrence, and high morbidity, it has commanded the attention of the profession since antiquity. In spite of countless investigations, leading to voluminous literature, on the subject, there are still blind spots in our knowledge of this condition. Medical science is always handicapped in its research because of the subjective nature of its material. Clinical observations are not as amenable to measurement as the changes which occur in a test tube, and frequently they are only the personal impressions of the observer. Subjective impressions are difficult to classify and compare. The physical examination of the clinician may lead to one diagnosis; the observations of the surgeon may lead to another; and both of these may be at variance with the findings of the pathologist. Hence, clinical reports often present widely different conclusions following apparently similar experiences. This has been especially true in the literature of acute cholecystitis. To the inherent difficulty in studying such a clinical problem is added the confusion of terminology—a term such as "early surgery," for example, having many different connotations. With these facts in mind, this study was undertaken.

An attempt was made to correlate in precise terms the clinical features, the operative pathologic findings, the postoperative course, and follow-up results in a well-studied series of cases. Special attention was given to the incidence and significance of jaundice and to the management of these cases of acute inflammation of the gall bladder.

A survey was made of all the patients with acute cholecystitis who were operated upon on the B and C surgical ward services of The Mount Sinai Hospital in the six years preceding 1945. It became obvious immediately that the clinical and operative impressions as to the severity of the inflammatory process were not always confirmed by the pathologic findings. Some gall bladders, especially when obstructed, may become filled with a thick pale bile, containing much mucus, which closely resembles pus. Fallis and McClure[1] reported that of forty cases in which the surgeon diagnosed empyema, only fifteen were actually proved pathologically. Therefore, in this study, only those cases were included in which the diagnosis of acute cholecystitis was made by the pathologist. The only exceptions were the few cases in which a cholecystostomy was done, and in which the diagnosis was, therefore, based on the gross findings at operation.

This series consists of 109 cases of acute cholecystitis. There were seventy-two women and thirty-seven men, a ratio of almost two to one for women. Their

Received for publication, June 22, 1946.

ages ranged from 17 to 72 years for the women, with an average of 50, and from 25 to 72 years for the men, with an average of 52.

Previous History.—The vast majority (91 out of 109) of these patients had previous symptoms of gall bladder disease. These consisted of either attacks of colic or typical gaseous dyspepsia, or both. Chills were only an occasional accompaniment of colic. Thirteen of these patients gave a history of jaundice prior to the acute attack for which they were operated upon. The history of icterus is not reliable because it depends on subjective description. A description of "dark urine" was not accepted alone as evidence of a history of jaundice. Acceptable histories were only those in which the patient described a definite yellow color of the skin, but even these may have been subject to error. Pruritus was mentioned too infrequently to be of significant help in diagnosis. Eighteen of the patients, that is, about one in six, experienced the first attack of gall bladder pain at the time of admission. All but one of these eighteen patients had stones present at operation. These calculi must have been present for a varying length of time prior to the initial attack, thus reiterating the well-known fact that a cholelithiasis does not always give rise to clinical manifestations. Three of the patients in the series gave a definite history of typhoid fever, which is a higher incidence than one would expect in the general population, and speaks for its etiologic importance in some cases.

Physical Findings.—Practically all patients had tenderness of varying degree in the right upper quadrant of the abdomen. Rigidity and rebound, which usually paralleled each other, were present in approximately one-half the cases. In twenty-eight cases the gall bladder was definitely palpable, and in twenty-one others there was a questionable mass which could not be identified definitely as gall bladder. One interesting feature was the presence of a palpable enlarged liver in twenty-three cases, or almost one-quarter of the total.

Laboratory Findings.—From Table I it is evident that the incidence of gangrene is higher in those cases in which the temperature was over 102° F. and the white blood count was more than 15,000. There were some cases in which temperature and white count were elevated above these arbitrary figures and in which the inflammatory changes were very severe; however, since the pathologist did not report them as gangrenous, they were not included. In other cases of gangrenous cholecystitis the white count and temperature were only slightly below the arbitrary level of 15,000 and 102° F. Thus, the correlation between temperature and the elevated white count, and degree of inflammation in the

TABLE I. LABORATORY FINDINGS

	NUMBER OF CASES	INCIDENCE OF GANGRENE OF GALL BLADDER	PER CENT OF GANGRENE
All cases	109	22	20
Temperature under 102° F.	83	10	12
Temperature 102° F. and over	26	12	46
W.B.C. under 15,000	74	8	11
W.B.C. 15,000 or over	35	14	40
Temperature over 102° F. *and* W.B.C. over 15,000	12	7	58

gall bladder is even greater than the figures indicate. One can say with some assurance that in the presence of a temperature over 102° F. and white blood count over 15,000 there is at least an even chance that one will find a severe acute cholecystitis and often actual gangrene. However, the converse of this statement is not necessarily true, for in a previous study in this hospital, Touroff[2] has shown that many acutely inflamed gall bladders, especially when subsiding, will have few or no clinical manifestations.

Operation.—In general, so-called early operation was performed on these patients. Early operation is an indefinite term, used here to mean operation within one to three days after admission. Since the majority of patients had been ill for an additional one to three days prior to admission, it follows that operation was performed in from two to six days after the onset of the illness. Many were operated upon the first hospital day, there being being only enough delay to confirm the diagnosis and prepare the patient adequately for surgery. In a few cases, operation was delayed several days to a week or more, usually because the diagnosis was not certain and conservative therapy was deemed wiser.

Of the 109 patients subjected to operation, ninety-six had a cholecystectomy and thirteen a cholecystostomy. Cholecystostomy was done only in severely ill and aged patients. Five of these patients were jaundiced, two had perforations of the gall bladder with a bile peritonitis, two others had gangrenous gall bladders, and the remainder were acutely ill with associated degenerative diseases. In this group of thirteen patients there were two deaths. One of these occurred in a 67-year-old patient with diabetes who had a perforated gall bladder with peritonitis, and who developed a hemiplegia three days postoperatively; the other was in a 68-year-old woman with marked jaundice, in poor general condition, who died on the operating table. This high mortality is indicative of the extremely serious condition of these patients, rather than the danger of the operative procedure. It is occasionally stated that cholecystostomy has as high or higher mortality than cholecystectomy but cholecystostomy is done only on the poor-risk patients, on whom any operative procedure will produce a high mortality.

Of the eleven patients who survived after cholecystostomy, one had a partial cholecystectomy by sloughing portions of a gangrenous gall bladder following operation, two returned within one year for cholecystectomy, the remaining eight patients have remained well to date. This observation is in accord with Elliason and Stevens,[3] who reported that following cholecystostomy for acute cholecystitis, 84 per cent of patients remained well. While cholecystostomy is not the procedure of choice for acute cholecystitis, it has definite indications and is often followed by good results.

Cholecystectomy was performed in ninety-six patients in this series. Drainage to Morison's pouch was used routinely in all cases. In seven of these cases a choledochostomy was performed. Five of these patients who were jaundiced will be considered separately. In the remaining two patients who were not icteric, the ducts were dilated, one caused by a palpable stone, and in the other nothing was found to account for the dilatation. In this group of ninety-six

patients, many of whom were acutely ill and had other associated chronic diseases, there were two deaths, or a mortality of less than 2 per cent. One was a woman, aged 67 years, who was jaundiced and had a cholecystoduodenal fistula. She developed a positive blood culture after operation, and the post-mortem revealed multiple liver abscesses. The other was a man, aged 64 years, who, following the removal of a gangrenous gall bladder, developed paralytic ileus and a wound dehiscence. No post-mortem was obtained in this case.

Pathology.—Of the 109 cases in this series, 106 patients, or over 97 per cent, had stones in the gall bladder and three did not. This is a somewhat higher incidence of stones than is usually reported,[1] but it emphasizes the general rule that stones are present in the vast majority of cases of acute cholecystitis.

TABLE II. ONE HUNDRED NINE CASES

	ACUTE GANGRENOUS CHOLECYSTITIS	PER CENT	ACUTE NONGANGRENOUS CHOLECYSTITIS	PER CENT
Cases	22	20	87	80
Positive bile culture	13	59	24	28
Bacillus coli	9	69	15	63

In Table II are compared the results of bile culture in the gangrenous and nongangrenous gall bladders. Of the twenty-two gangrenous gall bladders, thirteen, or 59 per cent, had a positive culture, while of the nongangrenous cases only twenty-four out of eighty-seven, or 28 per cent, had a positive culture. In other words, positive cultures are obtained twice as frequently in the gangrenous as in the nongangrenous. One might infer, therefore, that bacterial infection plays a major role in the gangrenous cases, and a minor role in the others. However, it is well known that bile inhibits bacterial growth, and that a negative culture is due more to this inhibitory action than to the absence of bacteria. Furthermore, the bacteria which are present in the lumen of the gall bladder are not necessarily responsible for the infectious process in the wall. Many workers have shown that cultures taken from the gall bladder wall are positive in a much higher percentage of cases than from the lumen, and usually grow out a streptococcus, whereas in the lumen the usual organism is Bacillus coli. Rosenow[4] and Magner and Hutcheson[5] all believe that streptococci are the most important etiologic agents in cholecystitis and that *B. coli* cultured from the lumen is a secondary invader. In this connection it is interesting that in the present series *B. coli* was present in the bile of the gangrenous and nongangrenous gall bladders in almost equal percentages, namely 69 and 63, respectively. This lends indirect support to the theory that *B. coli* in the lumen may not be concerned with the inflammatory process in the wall, but is only a secondary invader.

It is not easy to explain why some cases of acute cholecystitis progress to gangrene. In several of these cases, a stone was impacted in the cystic duct. Such an obstruction should increase tension within the gall bladder, until there is interference with the blood supply, and gangrene develops[6]; or an impacted stone may interfere with the venous returns from the gall bladder, and thus contribute to development of gangrene. However, this does not explain those

cases in which the stones are not impacted or the occasional case of noncalculous gangrenous cholecystitis. In this connection, Colp and Doubilet[7, 8] and others[9, 10] have drawn attention to the clinical significance of pancreatic reflux. They have reported cases of acute noncalculous cholecystitis which were probably due to the necrotizing effect of an activated pancreatic reflux.

Jaundice.—The clinical significance of jaundice in acute cholecystitis was one of the prime objects of this study. In reviewing the cases it was not always easy to decide just what constituted jaundice. In those cases in which there was a definite discoloration in the skin and mucous membranes, laboratory results were usually confirmatory and there was no question as to the jaundice. However, some patients had an increase in icterus index, without bile in the urine, whereas others had detectable bilirubin in the urine, without an elevated icterus index. It was found that a number of patients showed the transient presence of bilirubin in the urine one or two days postoperatively, with prompt disappearance thereafter. Therefore, the criterion which was established for jaundice was an icterus index of 10 or more, together with bilirubin in the urine, and with or without visible icterus in the skin and mucous membranes. In this way, six patients who had icterus indices ranging from 10 to 15, but without bile pigment in the urine, were omitted from consideration, and two with bile in the urine on a single determination but no elevation of icterus index or clinical jaundice were also omitted. It was felt that possible errors in laboratory work would be overcome by these standards.

Nineteen patients in this series fulfilled the criterion of jaundice at the time of operation. This was an incidence of 17 per cent. Six of these patients, or approximately one-third, had a previous history of jaundice, and the remainder were jaundiced for the first time. The ages of the patients varied from 32 to 72 years, with a mean of 56, which is somewhat higher than the average for acute cholecystitis in general. The duration of dyspepsia or colic prior to the attack for which the patient was admitted was very variable and there was no apparent correlation between duration of symptoms and jaundice. However, the majority of the patients had had symptoms for less than four years.

A comparison was made between the clinical and laboratory findings in these jaundiced patients with those found in the group as a whole.

TABLE III

	NUMBER OF PATIENTS	PALPABLE GALL BLADDER	PER CENT OF PALPABLE GALL BLADDER	PALPABLE LIVER	PER CENT OF PALPABLE LIVER
Jaundiced	19	9	47	6	31
Nonjaundiced	90	19	19	17	19

Reference to Table III shows that palpable gall bladders were present in almost one-half the jaundiced patients, and more than twice as frequently as in the nonjaundiced. Similarly, the ratio of palpable livers was 31 to 19 per cent, respectively.

There was no significant characteristic to the temperature or white count. Eleven of the patients had a temperature of less than 102° F., and eight were

over 102° F. Thirteen had white blood counts of less than 15,000 and six were over 15,000.

Liver function tests were done in two-thirds of the cases. These were either cephalin flocculation or cholesterolesters, or both. In one-half the cases in which these tests were done, the laboratory results indicated liver damage. Liver function determinations are notorious in their fluctuation and difficulty of interpretation. A certain number of "normal" individuals in the older age group will show an abnormal response to these tests. Therefore, the findings in this series must be considered as suggestive of liver damage, rather than conclusive. Even if actual liver damage is present in any case, it is not certain that this is due to an hepatitis. The coexistence of hepatitis and cholecystitis is postulated by numerous writers.[11, 12] However, this relationship has been questioned by Colp and associates,[13] who found that when biopsies were aspirated from the liver depths, and subjected to careful histologic study, the liver cells showed no changes in cases of cholecystitis without jaundice. In cases with jaundice, there was a focal liver cell degeneration, which represents a reaction to bile stasis rather than a direct relation to the primary disease in the gall bladder. It would seem, therefore, that when liver damage is present in a patient with cholecystitis, it is a secondary effect of obstruction rather than a direct accompaniment of the gall bladder disease.

Of the nineteen jaundiced patients, thirteen had a cholecystectomy and six had a cholecystostomy. Only three of the nineteen had gangrenous gall bladders, which is a somewhat lower incidence than for the group as a whole. This would seem to indicate that jaundice is not necessarily associated with a severely inflamed gall bladder.

The common bile duct was enlarged in six cases and normal in the remaining thirteen. The dilated ducts were explored. Stones were found in five patients. In two of these no stones were palpable, but a choledochotomy was instituted because of the dilatation and jaundice, and small stones were found. Such incidents prove that palpation alone cannot be used as an index to the presence of stones.

Of these six jaundiced patients who had explorations of the common duct, one died with liver abscesses and septicemia evidently due to a suppurative cholangitis; one other patient in whom a cholecystostomy had been done continued to have colic. Reoperation was performed within two years, a cholecystectomy was done for chronic cholecystitis, and stones were again removed from the common duct. Thereafter, he did very well. The remaining four patients in this group made a good recovery and have remained well.

There were thirteen jaundiced patients in whom the common bile duct was not explored. The follow-up on these thirteen patients showed that five made excellent recoveries with an uneventful course thereafter. Three had fairly good results, with mild dyspeptic symptoms; two patients were lost to the follow-up clinic; one was an operative death previously mentioned. It is noteworthy that of the ten patients in this group who were followed, all obtained relief from the jaundice without exploration of the common duct. Only two patients had

recurrence of colic and jaundica within one and one-half years, and they were reoperated upon and the common ducts explored. In one of these patients, stones were found in the common duct and removed. In the other, the common duct was enlarged, but no stones were present. Both of these patients made an excellent recovery and have remained well since operation.

From these cases one can deduce that jaundice plus dilatation of the common duct demands exploration of the duct, since stones were found in five out of six such instances. However, jaundice, alone, in the presence of a normal common duct, is not an absolute indication. These patients are relieved of their jaundice following simple removal (or sometimes only drainage) of the gall bladder. In a small proportion (two out of ten) one can expect recurrence of jaundice and the necessity of a secondary operation. However, in the majority of cases they will remain symptom-free. Unfortunately, it cannot be predicted, at the time of the initial exploration, in which group the patients will fall, and it becomes a matter of judgment in deciding upon the procedure. In those cases in which the jaundice subsequently disappears without choledochotomy, one may ascribe the jaundice to small, nonpalpable stones which were passed spontaneously, to inflammatory edema around the duct which subsided, or to spasm of the sphincter mechanism incident to the acute cholecystitis.

Follow-up.—Among the 109 patients in this series, there was a total of four postoperative deaths, or a mortality of less than 4 per cent. The remaining 105 patients were followed for a period of one to six years. Adequate follow-ups were obtained in eighty-five cases, and in twenty there was no adequate follow-up. The results of treatment were arbitrarily divided into three groups—very good, fairly good, and poor. Seventy patients had very good results, meaning that they were symptom-free. Nine patients had fairly good results, signifying relief of pain, but persistence of some indigestion. In six cases the results were classed as poor, because of persistence of pain as well as indigestion. There were only three cases of noncalculus cholecystitis in this series, and among these the follow-up disclosed a poor result in one patient and a fair result in another. This is too small a group from which to draw conclusions. However, it has been observed repeatedly that patients undergoing cholecystectomy for noncalculus cholecystitis are especially prone to certain postoperative complaints which constitute the "post-cholecystectomy syndrome."[14] Some of these symptoms may have been due to a primary dyskinesia of the sphincter mechanism,[15] and, therefore, the removal of the gall bladder did not eradicate the major pathology, hence the higher incidence of postcholecystectomy symptoms in cases of noncalculus cholecystitis.

SUMMARY

1. In a study of 109 cases of acute cholecystitis, there was frequent correlation between the severity of inflammattory process in the gall bladder and the temperature and white count. Where the temperature was over 102° F. and the white blood count was over 15,000, the gall bladder was gangrenous in at least one-half the cases.

2. Cholecystectomy is the procedure of choice for acute cholecystitis, but even when cholecystostomy was done, the majority of patients remained symptom-free without any further surgery.

3. Stones were found in 97 per cent of acute cholecystitis.

4. Of the acutely inflamed gall bladders, 20 per cent were gangrenous. Gangrenous gall bladders had higher incidence (59 per cent as compared to 28 per cent) of positive bile cultures than nongangrenous, but the proportion of *B. coli* organisms was approximately the same (69 per cent versus 63 per cent). *B. coli* may be a secondary invader in the lumen of an inflamed gall bladder.

5. Gangrene of the gall bladder in some cases is due to obstruction of the cystic duct by stone, causing increased tension within the lumen, and interference with venous return. Noncalculus gangrene may be due to the necrotizing effect of an activated pancreatic reflux.

6. Of the acute cholecystitis cases, 17 per cent of the patients were jaundiced. The gall bladder and liver were enlarged more frequently in these cases than in simple acute cholecystitis. However, there was no conclusive evidence that hepatitis was a constant accompaniment of cholecystitis.

7. Jaundice plus a dilated common duct demands exploration of the duct because stones were usually found, even if not felt. However, jaundice without duct dilatation disappeared after simple operation on the gall bladder. In only two out of ten cases was there recurrence of jaundice necessitating a secondary operation. Only one of these patients had stones in the common duct, the other having an enlarged duct without stones.

8. Persistence of dyspepsia after cholecystectomy may be due to a dyskinesia of the sphincter mechanism.

REFERENCES

1. Fallis, L. S., and McClure, R. D.: Acute Cholecystitis, Surg., Gynec. & Obst. **70**: 1022, 1940.
2. Touroff, A. S. W.: Acute Cholecystitis, Ann. Surg. **99**: 900, 1934.
3. Elliason, E. L., and Stevens, L. W.: Acute Cholecystitis, Surg., Gynec. & Obst. **78**: 98, 1944.
4. Rosenow, E. C.: Focal Infection and Elective Localization of Bacteria, Surg., Gynec. & Obst. **33**: 19, 1921.
5. Magner, W., and Hutcheson, J. M.: Cholecystitis: Bacteriological and Experimental Study, Canad. M. A. J. **27**: 469, 1932.
6. Saint, J. H.: Acute Obstructive Cholecystitis, Surg., Gynec. & Obst. **77**: 250, 1943.
7. Colp, R., and Doubilet, H.: Clinical Significance of Pancreatic Reflux, Ann. Surg. **108**: 243, 1938.
8. Colp, R., and Doubilet, H.: The Operative Incidence of Pancreatic Reflux in Cholelithiasis, SURGERY **4**: 837, 1938.
9. Bisgard, J. D., and Baker, C. P.: Pathogenesis of Cholecystitis, Cholelithiasis, and Acute Pancreatitis, Ann. Surg. **112**: 1006, 1940.
10. Gray, S. H., Heifitz, C. J., and Probstein, J. G.: Effect of Division of Sphincter of Oddi on the Bile Diastase of the Dog, Arch. Surg. **47**: 160, 1943.
11. Graham, E., and Cole, W. H.: Diseases of Gallbladder and Bile Ducts, Philadelphia, 1928, Lea & Febiger.
12. Weir, J. F., and Snell, A. M.: Symptoms That Persist After Cholecystectomy, J. A. M. A. **105**: 1093, 1935.
13. Colp, R., Doubilet, H., and Gerber, I. E.: The Relation of Cholecystitis to Pathologic Changes in the Liver, Ann. Surg. **102**: 202, 1935.
14. Colp, R.: The Post-Cholecystectomy Syndrome and Its Treatment, Bull. New York Acad. Med. **20**: 203, 1944.
15. Strode, J. E.: Biliary Dyskinesia From Surgical Viewpoint, Ann. Surg. **117**: 198, 1943.

INTRATHECAL PENICILLIN IN BACTERIAL MENINGITIS

ROBERT G. LIVINGSTONE, M.D., BOSTON, MASS., AND
JOHN E. LEACH, M.D., NEW YORK, N. Y.

(From the Head and Neck Department and the Department of Medicine of the Memorial Hospital, New York, N. Y.)

REPORTED experiences with the intrathecal administration of penicillin in bacterial meningitis are currently of considerable interest. Thus used penicillin has given promise of acting in many instances as a reasonably safe and effective therapeutic agent, but nevertheless by this route it has also led in certain cases to failures and to complications of such nature that the tentative recommendations usually made for its administration have not been generally accepted. A successful experience with penicillin administered intrathecally in large doses in bacterial meningitis prompts the following reports and comments.

CLINICAL REPORTS

Streptococcal meningitis developed as an acute postoperative complication in two patients recently subjected to radical surgical procedures on the head and neck service of the Memorial Hospital.

A clinical diagnosis of meningitis was made first in one patient on the eighth day following excision of recurrent carcinoma within the nasal cavity. Confirmatory evidence was afforded when cerebrospinal fluid obtained by lumbar puncture was shown to contain *Streptococcus viridans* in pure culture. Treatment by orally given sulfonamides and by intramuscularly administered penicillin in the usually recommended doses was immediately instituted. Clinical response was prompt and striking, but because of recurrent positive cerebrospinal fluid cultures direct instillation of penicillin into the subarachnoid space seemed indicated. By lumbar puncture, five daily doses of 100,000 units of sodium penicillin dissolved in 5 c.c. of cerebrospinal fluid were administered intrathecally. No untoward effects, with the possible exception of generalized convulsions of undetermined origin following the fourth and fifth injections, were observed. The patient was discharged home as cured fourteen days after the institution of intrathecally administered penicillin.

A more extensive procedure, involving excision of the right maxilla and exenteration of the right orbit, was associated in the other patient with inadvertent puncture into the subarachnoid space. A gauze pack moistened with penicillin solution was applied to the wound, and treatment by whole blood transfusion, intravenously given sulfonamides, and intramuscularly administered penicillin was ordered. By the third postoperative day unmistakable clinical signs of meningeal infection developed. Lumbar puncture was promptly performed, and turbid cerebrospinal fluid which clotted readily was obtained under an abnormally elevated pressure. Through the same needle 50,000 units of

Received for publication, June 21, 1946.

sodium penicillin freshly dissolved in 5 c.c. of normal saline solution was at once instilled into the subarachnoid space. Initial cultures yielded a pure growth of *Streptococcus hemolyticus* (group A). Clinical response again was prompt, and after one week of uneventful daily treatment by this route the intrathecal administration of penicillin was discontinued. The patient has since then remained essentially well.

More detailed information concerning these patients is presented in the accompanying case reports.

CASE REPORTS

CASE 1.—The patient was a white woman 59 years of age who was admitted to the hospital on Dec. 19, 1945, because of recurrent epidermoid carcinoma within the nasal cavity. Almost two years previously the cartilaginous part of the lower two-thirds of the nose had been excised, the nasal septum and a large portion of the upper plate of the hard palate had been removed, and the anteromedial half of the right maxilla had been resected. Wide excision of the area of recurrent disease was carried out under intravenous sodium pentothal anesthesia on Dec. 21, 1945. During this procedure the cribriform plate of the ethmoid bone was exposed, and curettage of the ethmoid and sphenoid sinuses was performed. A gauze pack moistened with sodium penicillin solution was applied to the surface of the wound.

The immediate postoperative course (Fig. 1) was uneventful until a severe frontal headache developed on the evening of the third day. The following morning the patient was found moaning and thrashing about violently in bed, completely disoriented and uncooperative. The temperature was 102° F., and the blood pressure was 160/70. The wound margins were reddened, and both malar areas were slightly edematous. There was no nuchal rigidity. All abdominal reflexes, except for a transient reaction in the right upper quadrant, were absent. The deep tendon reflexes were hyperactive but equal bilaterally. An equivocal right Babinski response was obtained. Roentgenographic examination of the chest showed no relevant abnormalities.

A tentative diagnosis of encephalitis, attributed to retrograde extension of septic thrombosis from the operative site, was made. Sulfathiazole was given by mouth in an initial dose of 2 Gm. and a maintenance dose of 1 Gm. every four hours, and sodium penicillin was given intramuscularly in doses of 30,000 units every three hours. Within a few hours the patient was cooperative and well oriented, but she continued to complain of persistent frontal headache. The fever slowly subsided, and sulfadiazine was given in place of sulfathiazole.

On the seventh day the temperature rose to 103° F., and the blood pressure was found to be 220/120. No localizing neurologic signs were present. Lumbar puncture was performed, and clear, colorless fluid under a pressure of 250 mm. of water was obtained. There was no evidence of lumbar block. Quantitative cell counts were not obtained, but microscopic examination of the uncentrifuged fluid showed 22 polymorphonuclear cells per high power field. A differential white blood cell count showed 90 per cent polymorphonuclear cells, 3 per cent monocytes, and 7 per cent small lymphocytes. The temperature twenty-four hours later was 101° F., and the blood pressure was 180/70. Slight nuchal rigidity was present, and a positive Kernig's sign was found. There was a Babinski response on the right side. A second lumbar puncture was performed, and slightly cloudy fluid under a pressure of 300 mm. of water was obtained. Cultures of the previously withdrawn fluid showed a pure, heavy growth of *Str. viridans*. The dose of sodium penicillin was increased to 80,000 units every four hours.

The signs of meningeal irritation largely disappeared by the ninth day. The temperature was 98.6° F., and the blood pressure was 118/80. A number of transfusions of whole blood were given, and continued improvement was noted clinically in the ensuing seven days. The differential white blood cell count at the end of this time showed 85 per cent

polymorphonuclear cells, 1 per cent monocytes, and 14 per cent small lymphocytes. Adequate blood and cerebrospinal fluid concentrations of sulfonamide had apparently been attained. Roentgenographic examination of the skull showed generalized cloudiness of the sinuses and localized areas of bone destruction, presumably postoperative, in the nasal and ethmoid regions.

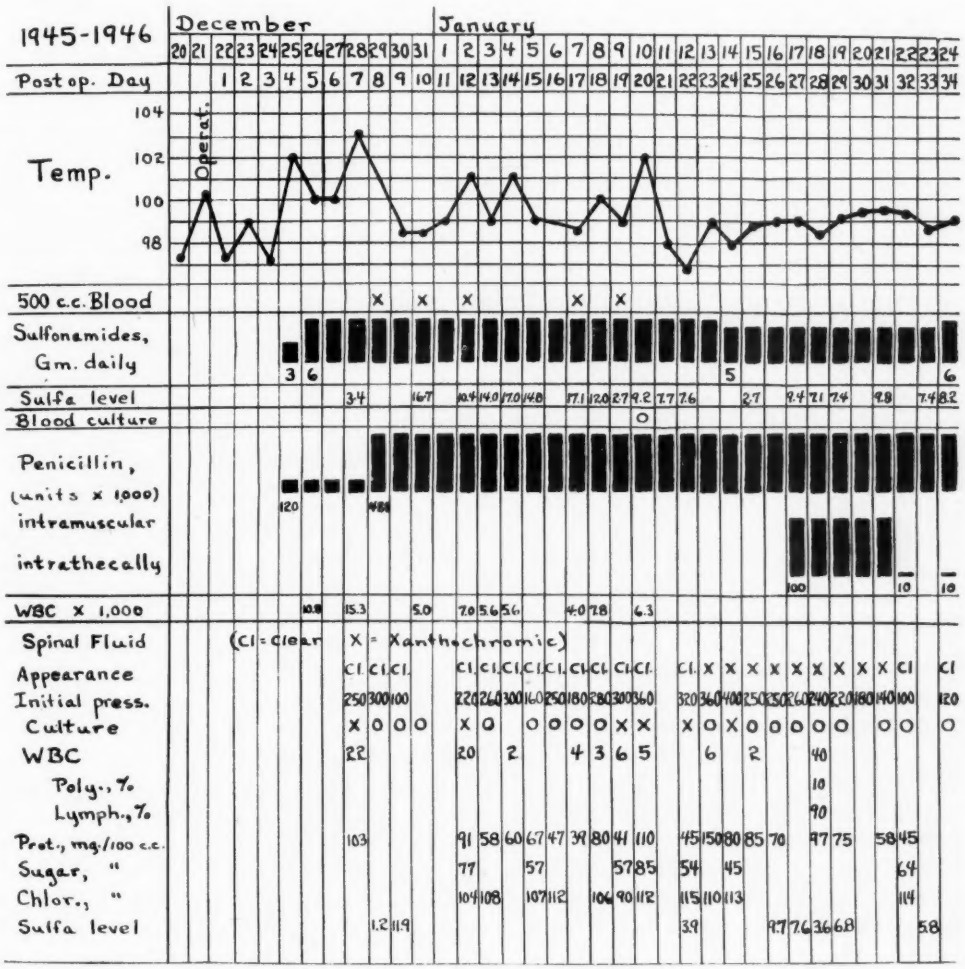


Fig. 1 (Case 1).—Hospital course, Dec. 20, 1945, to Jan. 24, 1946.

An episode of nausea and vomiting suddenly occurred on the eighteenth day, and the patient again complained of persistent frontal headache. The wound surface was clean and covered with healthy granulation tissue. Mild bilateral papilledema with blurring of the nasal fields and with some tortuosity of the veins was noted. On the twenty-third day xanthochromic cerebrospinal fluid under a pressure of 360 mm. of water was obtained by lumbar puncture. Microscopic examination of an uncentrifuged specimen showed 6 polymorphonuclear cells per high power field and 1,360 polymorphonuclear cells per cubic millimeter. No assays of the penicillin levels in the cerebrospinal fluid were made, and no determinations of the sensitivity of the infecting organisms to penicillin were carried out. An attempt was made to maintain adequate sulfonamide levels by administering sodium sulfadiazine intravenously in doses of 2.5 Gm. twice daily.

Cultures from the ethmoid and sphenoid sinuses at this time showed heavy growths of *Str. viridans* and scattered colonies of nonhemolytic *Staphylococcus aureus, Aerobacter aerogenes,* and nonhemolytic gamma Streptococcus.

The necessity for more aggressive treatment became apparent as clinical improvement failed to occur. Cultures of cerebrospinal fluid taken on the nineteenth, twentieth, twenty-second, and twenty-fourth days were reported as positive on the twenty-fourth, twenty-sixth, twenty-sixth, and twenty-seventh days, respectively. On the twenty-seventh day as a freshly made solution of 100,000 units of sodium penicillin in 5 c.c. of cerebrospinal fluid was slowly injected into the subarachnoid space, and when no immediate ill effect was noted a series of similar daily injections by this route was instituted.

About seven hours after the fourth intrathecal injection of penicillin the patient suddenly cried out loudly and exhibited two generalized convulsions which together lasted one or two minutes. She bit her tongue and frothed slightly at the mouth. Her eyes were turned up and to the right. The pupils were round, regular, and equal. No localizing neurologic signs were found. In five minutes or less a period of somnolence supervened. The patient could be roused, but she was unable to speak. A few hours later she seemed to be her usual self, though she had no recollection of the convulsive episode.

This complication was attributed to the prolonged course of the meningitis rather than to the possibly toxic effect of the therapeutic agent. A fifth intrathecal injection of penicillin was administered on the following morning. About seven hours later the patient began to complain of fatigue and of dull frontal headache. Within a short time she was found curled up in bed with the sheets drawn over her head, conscious but drowsy and transiently disoriented. There was some cyanosis of the face and hands. Mild photophobia was noted. The left arm was held stiffly outstretched for one or two minutes. The pupils were dilated but round and equal. There was slight bilateral papilledema. The deep tendon reflexes were hyperactive and equal bilaterally. The blood pressure was 160/80. No specific treatment was given.

On the following day there were no abnormal physical signs. The patient, however, was confused and disoriented in all spheres. She was quiet and cooperative, and she accepted food and medication without comment. Lumbar puncture yielded clear, colorless fluid under normal pressure and sterile on culture. As a provocative measure a dose of 10,000 units of sodium penicillin dissolved in 5 c.c. of cerebrospinal fluid was administered intrathecally. No untoward reactions were observed throughout the ensuing forty-eight hours.

Now considerably improved and well oriented the patient recalled her period of "forgetfulness" during the several preceding days. Temperature remained within normal limits. The white blood cell differential count showed 79 per cent polymorphonuclear cells, 2 per cent eosinophilic cells, and 16 per cent small lymphocytes. A second dose of 10,000 units of sodium penicillin was given intrathecally, and then all medication, including the sulfonamides and all intramuscularly administered penicillin, was arbitrarily discontinued.

Cultures of the sphenoid sinuses taken at this time showed *Monilia albicans, A. aerogenes, Staph. aureus,* nonhemolytic gamma Streptococcus, and *Str. viridans.* A small gauze pack moistened with isotonic saline solution was kept over the wound surface. No evidence of recurrent meningeal infection was noted. On the thirty-seventh day the patient was permitted to sit up, and within twenty-four hours she was out of bed and completely asymptomatic. Finally, on the forty-first postoperative day, fourteen days after the institution of intrathecally administered penicillin, she was discharged home as cured.

The patient was last seen on March 21, 1946. She was engaged in her normal pursuits, and she appeared to be in excellent health.

CASE 2.—The patient was a white woman 58 years of age, who was admitted to the hospital on Feb. 11, 1946, with a tumor of the right maxillary antrum of about four months' duration. Diplopia had been present for two or three days. Physical examination on entry showed slight proptosis of the right eye, slight swelling of the right cheek and right periorbital tissues, and an obstructing tumor in the right nasal cavity. Bone destruction of the

superior, medial, and lateral walls of the right antrum was demonstrable on roentgenographic examination. Tissue obtained by excision biopsy of the nasal portion of the tumor showed epidermoid carcinoma.

Radical removal of the tumor, involving excision of the right maxilla and exenteration of the right orbit, was carried out under intravenous sodium pentothal anesthesia on Feb. 15, 1946. During this procedure inadvertent entry into the subarachnoid space occurred, and cerebrospinal fluid was at once observed to be escaping freely from the puncture site. A gauze pack moistened with sodium penicillin solution was immediately applied to the area. Sodium sulfadiazine was given intravenously in doses of 2.5 Gm. twice daily, and sodium penicillin was administered intramuscularly in doses of 20,000 units every three hours.

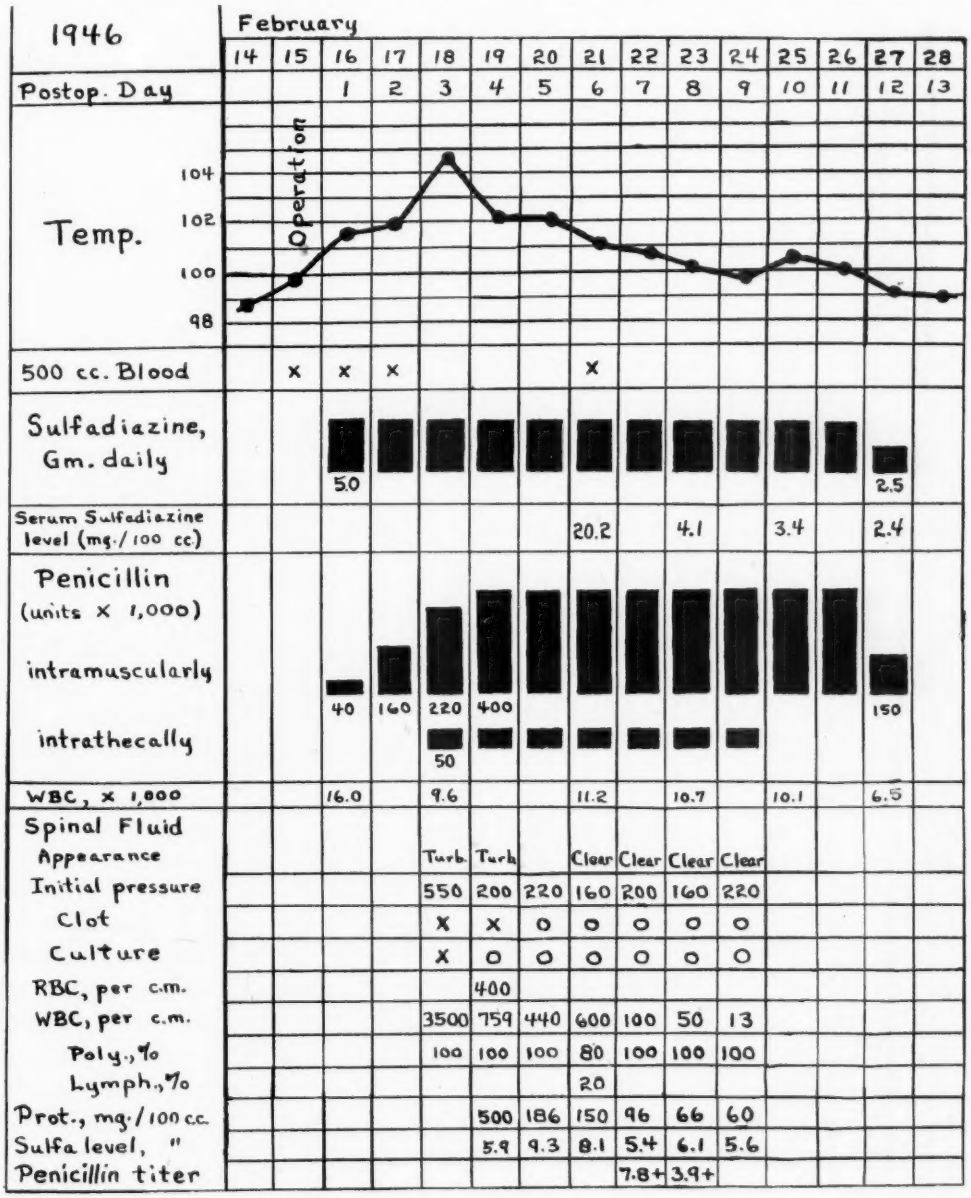


Fig. 2 (Case 2).—Hospital course, Feb. 14 to 28, 1946.

The immediate postoperative course (Fig. 2) was uneventful. On the third day the patient became noticeably quiet and unresponsive. A sudden chill occurred, and the temperature rose abruptly to almost 105° F. Examination then showed moderate nuchal rigidity and hypoactive, but bilaterally equal, deep tendon reflexes. The left retinal field was normal in appearance. There were no localizing neurologic signs. Lumbar puncture was performed, and turbid cerebrospinal fluid which readily formed a cobweblike clot was obtained under a pressure of 550 mm. of water. Through the same needle 50,000 units of sodium penicillin freshly dissolved in 5 c.c. of normal saline solution were slowly injected into the subarachnoid space. No untoward reactions were noted. The dose of intramuscularly administered penicillin was at the same time increased to 50,000 units every three hours.

The next day the patient was much improved, and the nuchal rigidity was appreciably diminished. Cultures of the previously withdrawn cerebrospinal fluid showed a pure, heavy growth of *Str. hemolyticus* (group A). A second dose of 50,000 units of sodium penicillin was administered intrathecally, and a series of daily injections by this route was instituted. On the seventh day estimation by a serial dilution method of the penicillin level in the cerebrospinal fluid twenty-four hours after the previous therapeutic administration by this route showed a concentration of 7.8+ units per cubic centimeter. The infecting strain of *Str. hemolyticus* (group A) was found to be inhibited by a concentration of 3.2 units per cubic centimeter but unaffected by a concentration of 1.6 units per cubic centimeter. On the following day similar examination of the cerebrospinal fluid showed a level of 3.9+ units of penicillin. A specimen of blood serum obtained at the same time, three hours after the preceding intramuscular injection, was found to contain 0.1 unit of penicillin per cubic centimeter.

When clinical improvement seemed assured and when no further positive cerebrospinal fluid cultures had been obtained for six days, the intrathecal administration of penicillin was discontinued. No evidence of persistent or recurrent meningeal infection was noted in the ensuing three days. Treatment with sulfonamides given intravenously and with penicillin administered intramuscularly was then also discontinued. The patient remained symptom-free, and on the twenty-eighth hospital day, twenty-one days after the institution of intrathecally administered penicillin, she was discharged home as well.

COMMENTS

Recourse to the intrathecal administration of penicillin in large doses to patients with bacterial meningitis presupposes careful consideration of the more commonly accepted methods by which effective, harmless concentrations of this therapeutic agent might be achieved and maintained in the cerebrospinal fluid.

Given intramuscularly in meningitis, penicillin, with all credit to earlier efforts in this direction, is not known to have been consistently demonstrated in the cerebrospinal fluid in concentrations adequate to inhibit strains of some of the pathogenic organisms which have been encountered.[3, 7, 12] Successful treatment of bacterial meningitis with penicillin administered by this route, alone or in conjunction with orally or parenterally given sulfonamides, has been reported,[10, 14] but evidence clearly supporting a definitive bacteriostatic action within the cerebrospinal fluid, rather than a more direct effect against a concurrent bacteremia or extrameningeal focus of infection, has not yet been offered.

The levels attained by the intramuscular route with doses considerably in excess of those usually recommended proved conspicuously ineffective in the patients reported here. The intramuscular administration of 8,640,000 units of sodium penicillin over an uninterrupted period of twenty-one days to the patient with *Str. viridans* meningitis failed to exert a noticeably adverse effect on the

infecting organisms in the cerebrospinal fluid. A heavy growth of *Str. viridans* was obtained within twenty-four hours from a specimen withdrawn by lumbar puncture at the end of this time. No assay of the penicillin concentration in the cerebrospinal fluid was attempted, however, and no determination of the sensitivity of the infecting organisms to penicillin was made. The administration of 300,000 units of sodium penicillin over an uninterrupted period of forty-eight hours to the second patient likewise failed to exert an appreciable effect on the organisms in the cerebrospinal fluid. Cultures of a specimen withdrawn when the first lumbar puncture was performed yielded a heavy growth of *Str. hemolyticus* (group A). As subsequent study later showed, the strain of infecting organism here encountered was relatively resistant to penicillin. An adequate concentration of the intramuscularly administered penicillin had apparently never been attained in the cerebrospinal fluid.

Given intravenously in bacterial meningitis, penicillin has not definitely been shown to have appeared in appreciable concentrations in the cerebrospinal fluid.[17] Single injections of various doses have been administered empirically to patients, but the reported results,[10, 14] while admittedly successful, have included no substantiating laboratory data.

More information is available concerning the concentrations of intravenously given penicillin in the absence of acute meningeal infection.[9, 11, 15] Significant levels in the cerebrospinal fluid, demonstrably effective against the commonly encountered infecting organisms, have not been attained with doses of ordinary magnitude, but titers approaching therapeutic requirements have been noted when doses of 10 to 25 million units,[15] administered over a twenty-four period by the intravenous drip technique, were utilized to breach the "hemato encephalic barrier."[9] The possible relationships between the total dose and the various body fluid concentrations thus suggested require further investigation.

Localized thrombophlebitis, more recently averted to some degree by recourse to the concurrent administration of heparin, has been reported as a hazard of the intravenous route,[1, 6] and systemic evidence of toxicity, manifested by nausea and vomiting or by the development of azotemia, has been mentioned as a consequence of massive dosage.[15]

Direct instillation of penicillin into the subarachnoid space in the absence of lumbar or ventricular block assures effective concentrations throughout the cerebrospinal fluid. The obvious advantage provided by this route of administration is reflected in the many successfully treated cases of bacterial meningitis which have been recorded.[2, 4-6, 13, 17, 19] Laboratory control, except initially in fulminating cases, is highly desirable to permit individualization of the general plan of treatment, and daily penicillin administration, utilizing a small volume of cerebrospinal fluid or sterile normal saline solution as the solvent, is probably best continued until satisfactory clinical response is evident and persistently negative cultures are obtained. Concurrent treatment with sulfonamides and intramuscularly administered penicillin is recommended to suppress the intensity of extrameningeal infection.[8, 17, 19] The possible acquisition of resistance to penicillin by the infecting organisms encountered, associated if it occurs with a corresponding decrease in virulence, need occasion no immediate concern.

Explanation elsewhere is probably required for the sporadic failures which have been described in the treatment thus outlined.[8]

Administration of penicillin by this route is not without its dangers and uncertainties. Many serious complications, transient or persistent in nature, have been attributed to this treatment.[9, 16-18] Meticulous care in choosing preparations of penicillin intended for intrathecal administration is requisite, and stringent precautions to prevent the various secondary infections which are known to have occurred is mandatory. The risk of repeated lumbar punctures in the presence of presumably elevated intracranial pressure must always be considered.[17] Only by achieving and maintaining harmless, as well as effective, penicillin levels may the objections to this treatment of bacterial meningitis be for the most part disregarded.[10]

The timely administration of penicillin intrathecally to the two patients reported here probably led to their prompt recovery. No apparent advantage was gained by utilizing doses in excess of those required to attain an effective cerebrospinal fluid level, but no known sequel occurred to warrant subsequent arbitrary limitation of any clinically indicated dosage. The occurrence here of generalized convulsions during the course of treatment of the first patient might justifiably be attributed to chronic central nervous system irritation by the disease alone. Recourse to a similar plan of treatment in the care of future patients under comparable circumstances thereby seems justified.

SUMMARY

Penicillin administered intrathecally in large daily doses led to the prompt, essentially uneventful recovery of two patients with postoperative bacterial meningitis, one of whom did not respond to an adequate trial of parenteral penicillin and sulfonamide therapy.

Penicillin administered intrathecally in the absence of lumbar block is recommended as a very satisfactory therapeutic agent in the treatment of fulminating or sulfonamide-resistant bacterial meningitis.

Grateful acknowledgment is made to Dr. William S. MacComb for permission to report these cases.

REFERENCES

1. Anderson, G. D.: The Treatment of Infections With Penicillin, New England J. Med. **232**: 400-405, 1945.
2. Cairns, H., Duthie, E. S., Lewin, W. S., and Smith, H. V.: Pneumococcal Meningitis Treated With Penicillin, Lancet **1**: 655-659, 1944.
3. Cooke, J. V., and Goldring, D.: The Concentration of Penicillin in Various Body Fluids During Penicillin Therapy, J. A. M. A. **127**: 80-87, 1945.
4. Fleming, A.: Streptococcal Meningitis Treated With Penicillin, Lancet **2**: 434-438, 1943.
5. Harford, C. G., Martin, S. P., Hageman, P. O., and Wood, W. B., Jr.: Treatment of Staphylococcic, Pneumococcic, Gonococcic and Other Infections With Penicillin, J. A. M. A. **127**: 253-259, 325-329, 1945.
6. Keefer, C. S., Blake, F. G., Marshall, E. J., Jr., Lockwood, J. S., and Wood, W. B., Jr.: Penicillin in the Treatment of Infections: Report of 500 Cases, J. A. M. A. **122**: 1217-1224, 1943.
7. McDermott, W., and Nelson, R. A.: The Transfer of Penicillin Into the Cerebrospinal Fluid Following Parenteral Administration, Am. J. Syph., Gonor., & Ven. Dis. **29**: 403-415, 1945.

8. Meads, M., Harris, H., Samper, B., and Finland, M.: Treatment of Meningococcic Meningitis With Penicillin, New England J. Med. **231**: 509-517, correction 680, 1944.
9. Neymann, C. A., Heilbrun, G., and Youmans, G. P.: Experiments in the Treatment of Dementia Paralytica With Penicillin, J. A. M. A. **128**: 433-434, 1945.
10. Price, A. H., and Hodges, J. H.: The Treatment of Meningitis With Penicillin Injected Intravenously and Intramuscularly, New York State J. Med. **44**: 2012-2014, 1944.
11. Rammelkamp, C. H., and Keefer, C. S.: Absorption, Excretion and Toxicity of Penicillin Administered by Intrathecal Injection, Am. J. M. Sc. **205**: 342-350, 1943.
12. Rammelkamp, C. H., and Keefer, C. S.: The Absorption, Excretion and Distribution of Penicillin, J. Clin. Investigation **22**: 425-437, 1943.
13. Rosenberg, D. H., and Arling, P. A.: Penicillin in the Treatment of Meningitis, J. A. M. A. **125**: 1011-1016, 1944.
14. Rosenberg, D. H., and Sylvester, J. C.: The Excretion of Penicillin in the Spinal Fluid in Meningitis, Science **100**: 132-133, 1944.
15. Schwemlein, G. X., Barton, R. L., Bauer, T. J., Loewe, L., Bundesen, H. N., and Craig, R. M.: Penicillin in Spinal Fluid After Intravenous Administration, J. A. M. A. **130**: 340-341, 1946.
16. Siegal, S.: Transverse Myelopathy Following Recovery From Pneumococcic Meningitis, J. A. M. A. **129**: 547-550, 1945.
17. Smith, H. V., Duthie, E. S., and Cairns, H.: Chemotherapy of Pneumococcal Meningitis, Lancet **1**: 185-193, 1946.
18. Sweet, L. K., Dumoff-Stanley, E., Dowling, H. F., and Lepper, M. H.: The Treatment of Pneumococcic Meningitis With Penicillin, J. A. M. A. **127**: 263-267, 1945.
19. Waring, A. J., Jr., and Smith, M. D. H.: Combined Penicillin and Sulfonamide Therapy in the Treatment of Pneumococcic Meningitis, J. A. M. A. **126**: 418-424, 1944.

INTRA-ARTERIAL PENICILLIN IN THE SURGICAL TREATMENT OF INFECTIONS OF THE EXTREMITIES

J. Ordie Shaffer, M.D., Minneapolis, Minn.

PENICILLIN has provided us with an effective antibiotic agent for the therapy of infections of the extremities. Unfortunately the problems of fibrous or osseous barriers and vascular impairment have frequently made high local concentration of penicillin unobtainable when given by the usual intramuscular or intravenous routes and the maximum beneficial effects hence have not been attained. Now, however, it has become possible to overcome some of these obstacles by the intra-arterial administration of penicillin. This method effectively overcomes the factors of tissue barriers and vascular impairment and facilitates a greater control of acute and chronic infections of the extremities.

Intra-arterial Therapy Discussion.—Intra-arterial administration of various drugs has been used since 1914 to obtain a high local concentration of the desirable therapeutic agent in the tissues supplied by the artery. In that year Heddaus[1] injected antitetanic serum via the carotid route seeking a maximum concentration of this serum in the cerebral tissues. Goyanes[2] injected the arteries of the extremities with a cyanate solution attempting to secure a high local concentration within tuberculous joints. Fiolle and Fiolle[3] injected hydrogen peroxide intra-arterially in dogs while investigating the possibilities of parenteral oxygenation. The results obtained by these men were not remarkable but they introduced this useful method of obtaining a high local concentration within the tissues. Subsequently, Dos Santos,[4, 5] Lamas,[6] De Fourmestraux,[7] Fredet,[8] Leriche,[9] Fritzsche,[10] Demel and Sgalitzer,[11] and Luccarelli[12] have utilized mercurochrome, colloidal silver, acriflavine, metaphen, gentian violet, and various other medicaments and serums. With the recent advent of more effective chemotherapeutic agents, Martinoff[13] employed prophylactically sulfanilamide and mercurochrome intra-arterially in extremity wounds with success. A. and E. Titelbaum,[14] Russian surgeons, reported a series of fifteen cases in which 100 to 150 c.c. of .85 per cent sulfanilamide were used intra-arterially with excellent results. E. Brancho Ribeiro[15] injected sulfanilamide intra-arterially for infections of the extremities and was the first to record the use of intra-arterial penicillin injections. In 1944 he stated, "Because our experience with intra-arterial sulfanilamide has been adequately long we are authorized to state that this method considerably diminishes the period of treatment in relation to other methods and it is to be expected that the same will happen with intra-arterial penicillin." Recently, Glasser and his associates[16] in this country have given penicillin intra-arterially, using the technique of Dos Santos,[5] in which a blood pressure cuff placed proximally on the extremity is inflated to a pressure of 280 mm. of mercury immediately following the injection and maintained at this pressure for ten minutes.

This thesis was submitted as part of the requirement for the degree, Master of Science in Surgery, March, 1946.

Received for publication, April 1, 1946.

Physiologic Considerations.—In consideration of the mode of administration and dosage of penicillin an important factor is whether the infection is primarily a generalized infection without abscesses (septicemia) or a local area of suppuration (abscess) that is relatively avascular. In a generalized infection without associated abscesses the effective bacteriostatic level of penicillin required in the serum as determined by the penicillin sensitivity of the infecting organism is the determining factor, whereas the permeability of the wall of the cavity to the penetration of the penicillin is the more important factor in a local lesion. Thus in a septicemia, the penicillin can be given by the usual intramuscular or intravenous routes of administration in variable dosages dependent upon the sensitivity of the causative organism. In a local lesion the permeability of the wall may be so reduced that even a very high concentration of penicillin in the serum remains ineffectual, and hence the mode of administration must be altered so that a higher penicillin concentration can be obtained locally. The more usual methods of administration of antibacterial drugs such as the oral, intramuscular, and intravenous routes are markedly less effective because of the dilution by the entire body fluids, and, second, because of both the local tissue barriers and vascular impairment in many of these cases. Topical application has proved somewhat effective superficially on wound surfaces but does not attain the penetration of the sites possible by the local or direct use as in the case of intrathecal, intra-articular, or intramedullary (bone) administration. Thus, in the case of an early acute empyema, penicillin given within the pleural cavity may bring about a good therapeutic result, whereas the usual modes of administration are ineffectual even though a high bacteriostatic level in the serum is present. The appropriate method of administration therefore depends upon whether the sensitivity of the infecting organism to penicillin or the permeability of the wall of the cavity is the more important. However, in the extremities of the body, many cases present involvement of a wide area, and the penicillin penetration becomes a problem either because of the impaired blood supply or the presence of infection within fascial or bony pockets. Intramuscular or intravenous administration is frequently ineffectual, and local administration becomes impractical both because of the large area involved and because of the presence of multiple small compartments. In this type of case the intra-arterial administration of penicillin has proved very effectual. When the penicillin is injected intra-arterially dilution remains minimal and the blood pressure forces the concentrated drug into the local area supplied by the artery. The distribution is further aided by the increased capillary permeability present in areas of local inflammation which permits a greater filtration of the agent locally.

The success of the arterial route was impressively shown, in a case reported by Fritzsche,[10] during therapy of a patient with generalized tetanus. Prior to therapy, the convulsions had been bilateral, but after one injection of serum into the left carotid, the convulsions almost disappeared on the right side but diminished very little on the left. This dramatically demonstrated the high concentration of medicament possible in the distribution of an artery injected.

The application of a tourniquet proximally to obstruct the venous return materially aids the increased local concentration of the drug. Thus, Goyanes[2] was able to obtain anesthesia of an extremity after injection of procaine intra-arterially only when he applied a proximal tourniquet after injection. When the tourniquet was not applied no anesthesia was obtained, and occasional toxic effects of the drug were observed indicating a return of a large portion of the drug into the general circulation. Dos Santos[4] demonstrated in arteriographic studies that the injection of sodium iodide into the brachial artery with a tourniquet applied proximally revealed the arterial shadow to be visible for fifteen minutes. Then "as the vessel loses its opacity, the tissues gradually become more accentuated, obviously due to the fixation of sodium iodide in the tissues."

In the present series of cases a new method of treatment has been introduced in that the blood pressure cuff is inflated to a subdiastolic blood pressure before the injection of the penicillin. This effectively prevents the return of venous blood and at the same time the continued arterial pressure aids in the distribution of the penicillin into the tissues without significantly increasing the dilution of the drug. With this technique a complete subsidence of inflammatory edema has usually occurred within twenty-four to forty-eight hours. Important in this regard is the finding of Lewis and Grant[17] that an increase in the arterial amplitude of their plethysmographic tracings occurred during the period of congestion produced by venous occlusion. More important, however, they noted a reactive hyperemia with an increase in arterial flow up to 600 per cent following the release of venous congestion after a period of compression at 80 mm. of mercury for fifteen minutes. Lewis[18] had also shown that the minute capillaries of the skin are able to contract against internal pressures of from 50 to 60 mm. of mercury. However, since petechial hemorrhages may appear if the venous pressure is raised to 90 to 100 mm. of mercury, the cuff is never inflated above 80 mm. of mercury in intra-arterial injections and in congested or ulcerated legs a value of 60 mm. of mercury is preferred.

Pumping the cuff to a high level above the systolic blood pressure following the injection is less efficacious since the benefits of venous hyperemia on the collateral circulation are not obtained and the propulsive force of the systolic pressure is lost.

TABLE I.—LISTING OF AGES AND WEIGHTS OF PATIENTS USED FOR THE DETERMINATIONS

METHOD	PATIENT	AGE (IN YR.)	WEIGHT (IN LB.)
Intravenous	H. B.	33	98
	J. C.	68	137
Intra-arterial	J. Z.	56	145
Cuff at 80 mm. Hg	J. O.	63	130
	O. T.	47	195
Cuff at 280 mm. Hg	M. L.	30	111
	H. S.	70	125
	F. P.	72	160
No cuff	T. E.	72	139
	J. B.	67	127

The comparative efficacy of the various intra-arterial methods and the intravenous method of injection were demonstrated by injecting radioactive phosphorus by various techniques and determining the concentration at various sites on the extremity by the Geiger counter.* Ambulatory patients with normal extremities were used to aid in ruling out the variability of circulatory impairment. In Table I are listed the ages and weights of the subjects used.

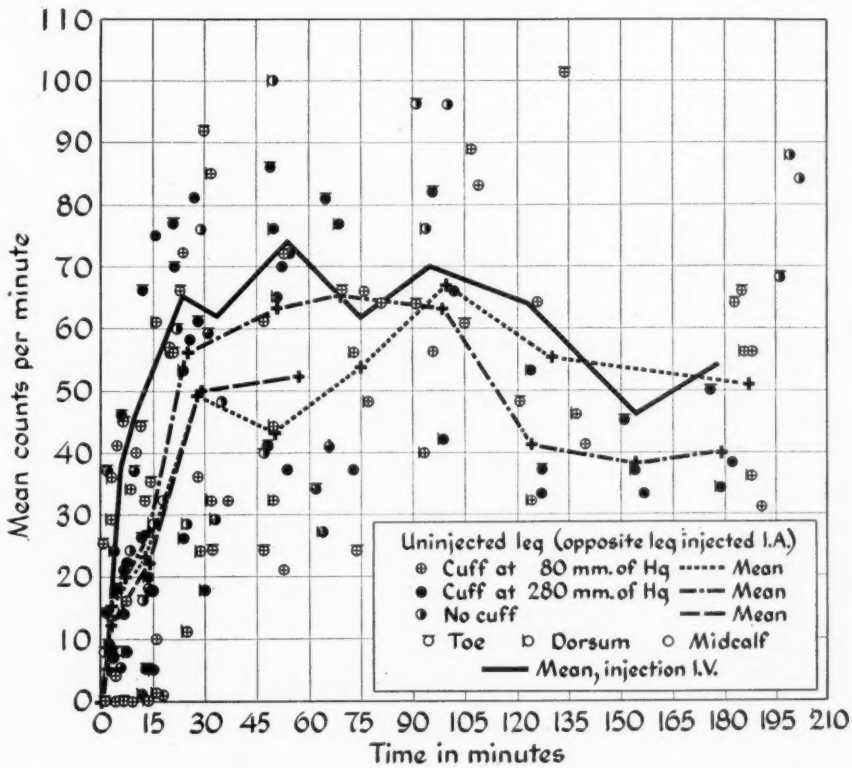

Mean counts per minute
Time in minutes
0 15 30 45 60 75 90 105 120 135 150 165 180 195 210
0 10 20 30 40 50 60 70 80 90 100 110
Uninjected leg (opposite leg injected I.A.)
Cuff at 80 mm. of Hg ····· Mean
Cuff at 280 mm. of Hg —·— Mean
No cuff — — Mean
Toe Dorsum Midcalf
Mean, injection I.V.

Fig. 1.—Radioactive phosphorus present in uninjected legs using the three different techniques of intra-arterial injection.

Four-tenths millicuries of radioactive phosphorus (P 32) in 10 c.c. of normal saline solution were injected intravenously, intra-arterially into the femoral artery without accompanying stasis by cuff, with the cuff at a subdiastolic pressure (80), and at a supradiostolic pressure (280) following the injection at a rate of 1 c.c. per second. These studies as illustrated by Figs. 1 to 5 revealed that all values taken by the intra-arterial method on the injected leg are over the mean for the intravenous method for a period of three hours, indicating that the intra-arterial method gives a higher local concentration in the leg than the intravenous method for this time. The maximum values obtained with the intra-arterial injection and the use of a blood pressure cuff for stasis remained over

*I am indebted to the members of the Radiation Therapy Department of the University of Minnesota Hospital, K. W. Stenstrom, J. F. Marvin, and S. Blank for their cooperation during the investigation with radioactive phosphorus and to the Physics Department of the Massachusetts Institute of Technology for having supplied the radioactive phosphorus.

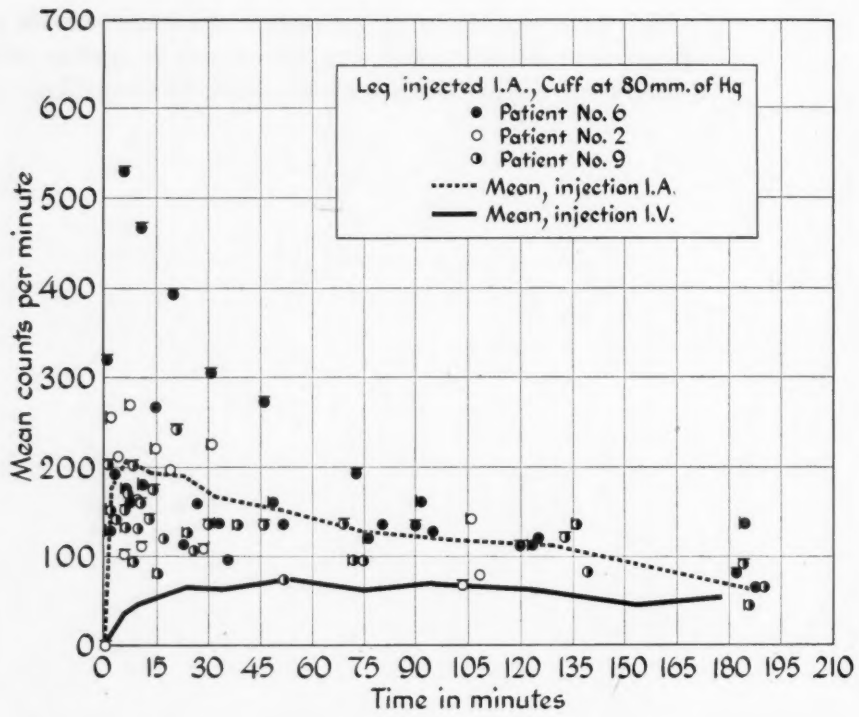


Fig. 2.—Radioactive phosphorus present in legs injected intra-arterially with blood pressure cuff at 80 mm. of mercury.

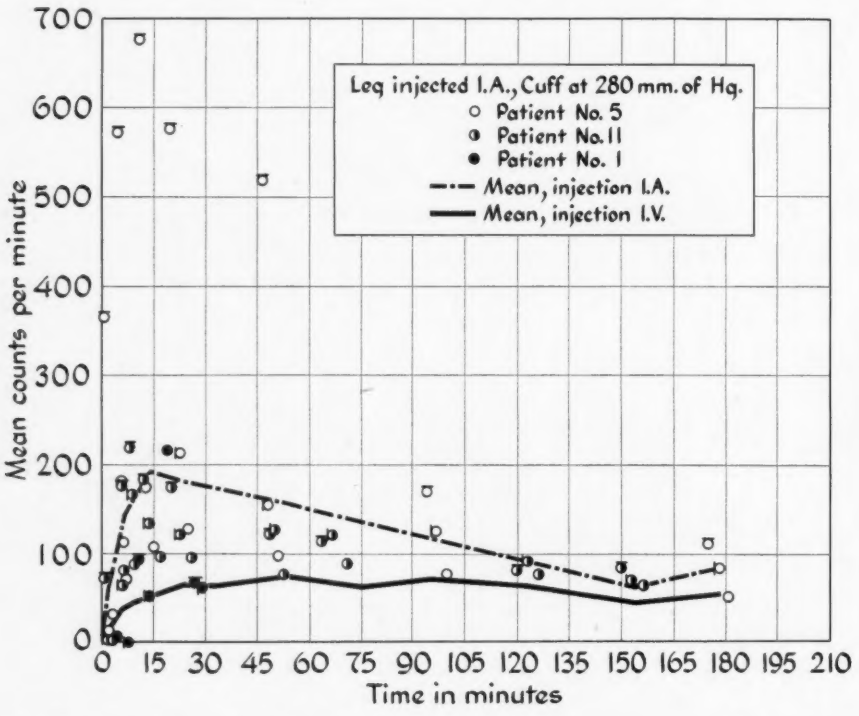


Fig. 3.—Radioactive phosphorus present in legs injected intra-arterially with blood pressure cuff at 280 mm. of mercury.

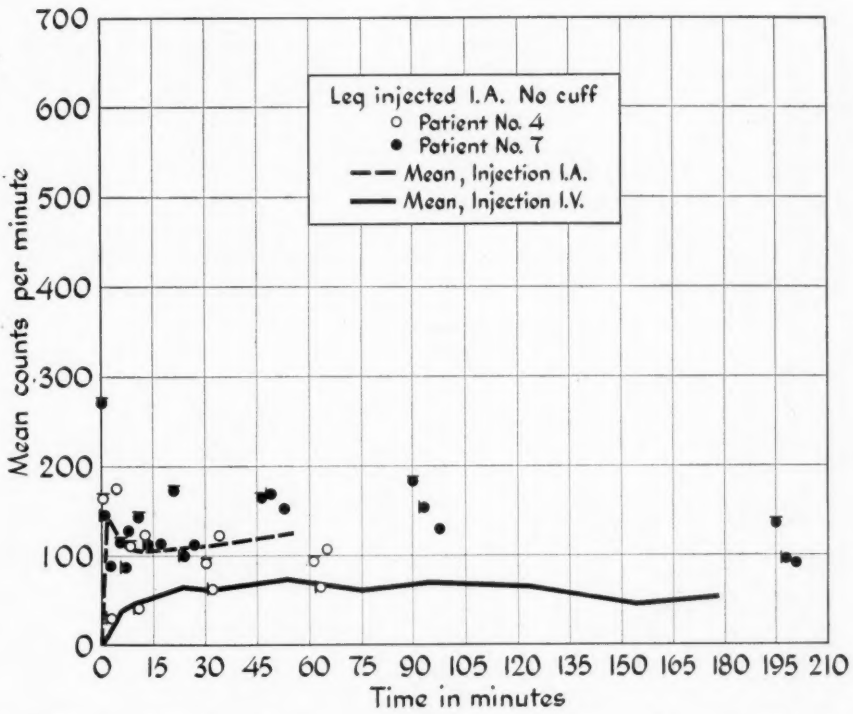


Fig. 4.—Radioactive phosphorus present in legs injected intra-arterially with no blood pressure cuff.

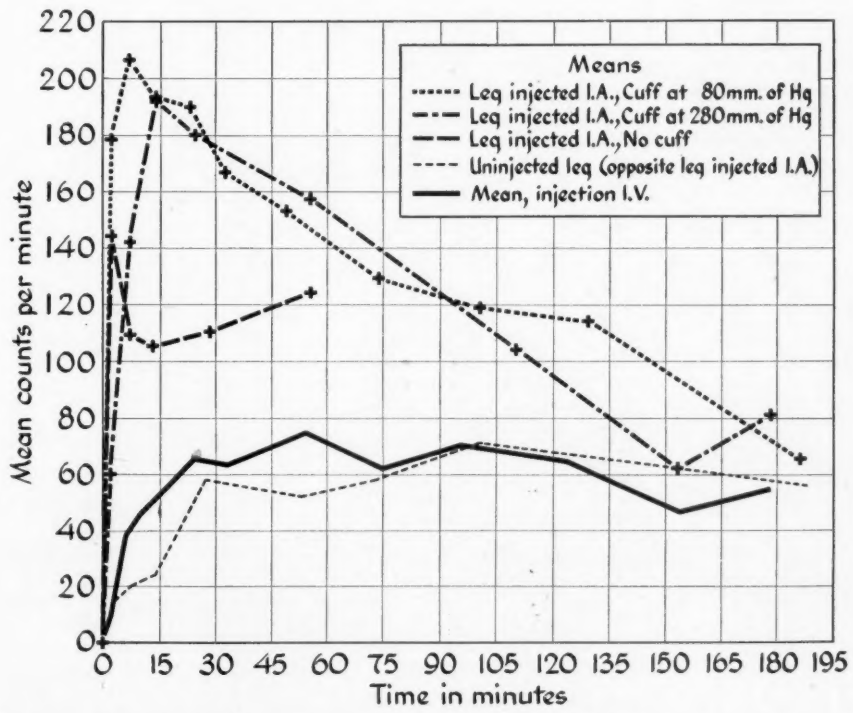


Fig. 5.—Mean curves of radioactive phosphorus present in injected legs using intravenous injection and the three different intra-arterial methods of injection.

TABLE II. MEAN VALUES OF GEIGER COUNTER DETERMINATIONS OF RADIOACTIVE PHOSPHORUS IN THE TOE, DORSUM, AND MIDCALF OF THE LEGS AFTER INTRAVENOUS INJECTION INTO THE LEFT ANTECUBITAL VEIN OF TWO NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	12	0	0
.5 to 3	10	2	10
4 to 7.5	8	6	38
8 to 12	8	10	46
19 to 28	10	24	65
31 to 36	10	33	62
51 to 56	4	54	74
71 to 80	11	75	62
90 to 100	12	95	70
120 to 127	12	123	64
150 to 157	6	154	46
170 to 187	10	178	54

TABLE III. MEAN VALUES OF GEIGER COUNTER DETERMINATIONS OF RADIOACTIVE PHOSPHORUS IN THE TOE, DORSUM, AND MIDCALF OF THE INJECTED LEG USING THE INTRA-ARTERIAL METHOD WITH THE CUFF AT 80 MM. HG IN THREE NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	9	0	0
.5 to 4	9	2	178
6 to 10	9	7	206
11 to 17	10	14	193
19 to 27	7	23	190
29 to 36	6	32	167
46 to 52	6	49	153
69 to 80	6	74	129
90 to 108	6	100	119
120 to 139	6	129	114
182 to 190	6	186	65

TABLE IV. MEAN VALUES IN THE TOE, DORSUM, AND MIDCALF OF THE INJECTED LEG USING THE INTRA-ARTERIAL METHOD WITH THE CUFF AT 280 MM. HG IN THREE NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	9	0	0
1 to 4	8	2	60
5 to 9	10	7	142
11 to 19	9	14	192
20 to 29	8	24	180
46.5 to 71	9	55	157
94 to 126	6	110	104
150 to 156	3	153	62
175 to 181	3	178	81

TABLE V. MEAN VALUES IN THE TOE, DORSUM, AND MIDCALF OF THE INJECTED LEG USING THE INTRA-ARTERIAL METHOD WITH NO CUFF IN TWO NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	6	0	0
.5 to 5	6	2	144
6 to 8	3	7	109
9 to 17	6	13	105
21 to 34	6	28	110
46 to 65	6	55	124

TABLE VI. MEAN VALUES OF GEIGER COUNTER DETERMINATIONS OF RADIOACTIVE PHOSPHORUS IN THE TOE, DORSUM, AND MIDCALF OF THE UNINJECTED LEG (OPPOSITE LEG INJECTED INTRA-ARTERIALLY) WITH THE CUFF AT 80 MM. HG IN THREE NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	9	0	0
1 to 5	9	3	15
6.5 to 7.5	3	7	20
9 to 18	11	13	23
20 to 37	12	28	49
47 to 53	6	50	43
70 to 81	6	75	54
91 to 109	6	100	67
121 to 190	6	130	55
183 to 191	6	187	51

TABLE VII. MEAN VALUES IN THE TOE, DORSUM, AND MIDCALF OF THE UNINJECTED LEG WITH THE CUFF AT 280 MM. HG IN THREE NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	9	0	0
1 to 4	7	2	5
5 to 9	6	7	20
12 to 18	8	14	27
20 to 30	9	25	56
48 to 54	6	51	63
65 to 73	3	69	65
96 to 102	3	99	63
121 to 127	3	124	41
151 to 157	3	154	38
176 to 182	3	179	40

TABLE VIII. MEAN VALUES IN THE TOE, DORSUM, AND MIDCALF OF THE UNINJECTED LEG WITH NO CUFF IN TWO NORMAL PATIENTS

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	6	0	0
1 to 6	6	3	12
10 to 18	6	14	22
22 to 35	6	29	50
47 to 66	6	57	52
91 to 100	3	95	89
106 to 202	3	199	80

TABLE IX. MEAN VALUES OF THE UNINJECTED SIDE OF ALL VALUES OF THE TOE, DORSUM, AND MIDCALF IN TABLES VI, VII, AND VIII

TIME INTERVAL	NUMBER OF VALUES	MEAN TIME	MEAN COUNTS PER MIN.
0	24	0	0
2 to 3	21	3	15
6 to 9	9	7	20
13 to 14	25	14	24
25 to 29	27	27	58
50 to 57	18	53	52
69 to 75	9	73	58
95 to 100	12	99	71
179 to 199	12	188	55

twice the maximum values obtained by injection without a cuff for a period of thirty minutes. The maximum values with a cuff fell to maximum values without a cuff at one and one-half hours, indicating that the stasis by the cuff gives a higher concentration locally for one and one-half hours. With the cuff at 280 mm. of mercury the minimum values remained below the mean for the intravenous method for thirty minutes, indicating that the phosphorus may be withheld from the leg in certain cases during this time. This suggests that the cuff at 80 mm. of mercury will give more consistent results.

Penicillin Dosage.—Fortunately, in infections of the extremities, the bacterial flora is usually sensitive to penicillin, and with a local infection of a portion of the body such as an extremity, the permeability of the local area is the determining factor. Therefore, the method of administration of the penicillin is the important variable rather than the dosage. On this basis an empirical dosage of 50,000 Oxford units of penicillin dissolved in 10 c.c. of saline solution has been used as suggested by Glasser and associates.[16] In several of the series, this dosage was given in 5 c.c. of saline solution, but since the dilution to 10 c.c. gives a solution with a pH equal to that of blood (7.4), the latter has been used recently, although no difference was noted clinically in the effects. The injections have been given once or twice daily. No improvement in the results was noted in cases in which intramuscular penicillin was given concomitantly.

Technique.—In most cases, particularly in those involving the feet and lower portion of the legs, a constant regimen is used. The patient is given 1 gr. papaverine hydrochloride hypodermically twenty minutes prior to the intra-arterial injection to aid in the vasodilation of the extremity since circulatory impairment is frequent in these cases. A second adjunct consists of soaking the foot (and leg) in a warm 1:9000 potassium permanganate solution for twenty minutes prior to the injection. This has the fourfold effect of aiding the cleansing and effecting better drainage in necrotic stumps, toughening the adjacent normal skin, and preventing maceration; second, it is one of the best fungicidal agents known and effectively controls the epidermophytosis, which frequently accompanies or in many cases actually causes the onset of the foot infection[19]; third, potassium permanganate acts as an excellent deodorant in gangrenous extremities[20]; and last, the warmth of the solution also aids as a temporary vasodilator immediately prior to the intra-arterial injection. For the injection, a 20 c.c. syringe with an attached 20 gauge needle 2½ inches long is used. A blood pressure cuff is placed just above the knee with the center of the cuff over the medial aspect of the thigh. The cuff is inflated to a subdiastolic blood pressure (60 to 80 mm. of mercury). With the surgeon standing on the right side of the patient the point of maximum pulsation of the femoral artery on the involved side below the inguinal ligament is palpated with the left hand, and the artery stabilized with the index and middle fingers (Fig. 6). The injection is done most easily in a plane perpendicular to the leg rather than at an acute angle. Proximity to the artery is noted by arterial pulsation transmitted to the syringe. A bright red stream pulsating into the syringe denotes that the needle is within the lumen of the artery. The color of the blood may vary in

different individuals but a good intermittent pulsation is taken as positive evidence of arterial blood. Care taken not to introduce the needle to too great a depth after getting within the lumen will obviate a transfixion of the artery and is easier than introducing the needle at an angle. Injections are done at a rate of 1 c.c. per second, and, immediately after withdrawal of the needle, digital pressure is applied over the site for a few seconds to obviate hematoma formation. In the case of the upper extremity, the blood pressure cuff is applied proximal to the infection (usually at some site above the elbow) and inflated to 80 mm. of mercury. Then the injection is made either at the brachial artery of the elbow or at the distal portion of the axillary artery. The blood pressure cuff is maintained at 80 mm. of mercury for ten minutes.

Although several of the patients have responded well to a total of only one or two injections, one or two doses daily are usually continued until optimal results are achieved.

Fig. 6.—Technique of intra-arterial injection; note pulsation of arterial blood into the syringe.

Therapeutic Application of Proposed Intra-arterial Regimen.—Intra-arterial penicillin and the proposed regimen have been used in forty cases of multiple types of infections of the extremities with excellent beneficial results. Diabetic gangrene and gangrene due to arteriosclerosis and frostbite with associated infection, osteomyelitis, suppurative joints, infected ulcerations of the legs and feet, and infected operative incisions have all responded well to this mode of therapy. Diabetic gangrene presents a problem in which the triad of diabetes, infection, and vascular impairment is met. Intra-arterial penicillin is presented as the most effective means of controlling the element of infection and will, of course, do the most for the patients with a severe infection who have an adequate circulation. After the infection has been controlled, several days may be devoted to improving the patient's general status by blood or plasma transfusions and a high protein regimen such as the Varco diet.[24] Amputation is considered

only after the patient has maintained a temperature below 99.6° F. for three days, the gangrene is well localized, and there is no surrounding inflammation in the normal tissues. A more accurate evaluation of the competence of the blood supply of the extremity can be carried out and the chance of success of a local procedure is increased. A major amputation may be done as an elective procedure at a lower amputation level with a lower mortality rate. Intra-arterial penicillin is given once daily during the first two to three postoperative days with a blood pressure cuff applied on top of the operative dressing and placed as high in the groin as permissible. The same technique of injection as previously used is then followed. Using this technique, an amputation, or extensive débridement is less frequently necessary. Since the effect of a chemotherapeutic débridement is accomplished, closure of the amputation stump can be done safely, and the patient is assured a better amputation stump. The case reports of eight patients with diabetic gangrene treated by this method are presented together with nine other illustrative cases.

CASE REPORTS

CASE 1.—C. M., an 88-year-old man with advanced arteriosclerosis, had a twelve years' history of diabetes and a six months' history of infection of the feet and gangrene. The gangrene had progressed to such a severity that the patient himself had pulled off the necrotic right second and third toes two weeks prior to admission. Physical examination revealed a severe wet gangrene with cellulitis and edema of the entire right foot. Purulent drainage exuded from the necrotic stump of the right foot where the toes had been avulsed. A wet gangrene of the third left toe and adjacent foot was also present. Culture of the purulent exudate revealed coagulase positive *Staphylococcus aureus*, and an x-ray examination of the right foot revealed osteomyelitis of all of the metatarsal bones. Evidence of severe arteriosclerotic heart disease was present including a left bundle branch block on electrocardiogram, so that the medical consultant thought that the patient's condition would not stand a major amputation and advised conservative management if at all possible. Intra-arterial penicillin (50,000 units), papaverine, and potassium permanganate foot soaks were given twice daily over a period of eleven days (twenty injections), during which time all drainage ceased, and the necrotic areas on both feet sloughed spontaneously. Penicillin packs (250 units per cubic centimeter) were placed locally on the clean granulation tissue, and healing occurred on both feet prior to discharge after twenty-two days' hospitalization. The patient has been ambulatory during the entire five-month period since discharge. Roentgenograms of the feet taken three months after the hospital discharge revealed senile osteoporosis and calcification of the vessels, and a bony absorption of the terminal phalanx of the left middle toe, but no evidence of any osteomyelitis previously present.

Two months after hospital discharge, a slight recurrent cellulitis of the dorsum of the foot was noted in the outpatient department, and he was placed in a rest home and given intramuscular penicillin, 20,000 Oxford units, every three hours by a nurse for seven days without improvement. Intramuscular penicillin was discontinued the second week and then given again during the third week with a slight progression of the cellulitis. The patient was then given one injection of 50,000 units of penicillin intra-arterially as an outpatient procedure, and the cellulitis completely disappeared in two days. The right foot has remained healed since that time.

Comment.—The greater efficacy of the intra-arterial route of penicillin administration is well demonstrated by the healing in this case of severe wet gangrene and osteomyelitis without surgical intervention and the subsequent

eradication of a recurrent cellulitis which had progressed over a three-week period while the patient was given well over 2 million units of intramuscular penicillin.

CASE 2.—H. R., a 65-year-old woman, had diabetic arteriosclerotic gangrene of the right third toe, cellulitis and edema of the entire right foot, a destructive osteomyelitis of all the phalangeal bones of the third toe and second and third metatarsals, and a temperature of 100.4° F. Routine intra-arterial penicillin therapy was given twice daily for four days at which time the edema and cellulitis had disappeared from the foot. A local amputation of the third toe was done and an adjacent sinus tract and abscess were opened. The cartilage on the articular surface of the third metatarsal was curetted but the metatarsals involved by osteomyelitis were not otherwise disturbed. Five intra-arterial injections of penicillin were given during the first four postoperative days, and the wound was very clean at that time. The only further therapy was the application of sterile dressings. The end of the foot was completely healed three weeks postoperatively, and the patient has been ambulatory during the four months since that time.

Comment.—Control of soft tissue infection and osteomyelitis made possible a successful local amputation in this case.

CASE 3.—G. Y., a 66-year-old woman, had diabetic arteriosclerotic gangrene with vesiculation and necrotic ulcerations of the foot and lower right leg, and edema, increased heat, mottling, and palpable venous thromboses extending to the upper third of the right leg. The temperature was 103° F. and the pulse was 120 per minute. An abscess on the lateral side of the foot was opened and the patient given intra-arterial penicillin twice daily; the temperature stayed below 99.6° F. after forty-eight hours of therapy. A local amputation on the foot was done on the fourth day but an ischemic necrosis continued to progress although no infection was present. A supracondylar amputation was then done with primary closure of the wound after an intra-arterial penicillin injection had been given immediately preoperatively. Adequate preoperative preparation of the patient made possible a smooth operative course with little change in the pulse or blood pressure in spite of the fact that no blood or plasma was used during the procedure or postoperatively. The stump healed by primary intention in ten days.

Comment.—Preoperative control of infection in this toxic case of diabetic gangrene by intra-arterial penicillin facilitated surgery and permitted primary healing of the closed amputation.

CASE 4.—H. B., a 63-year-old man, had diabetic gangrene with pitting edema and erythema of the entire left foot, a deeply penetrating necrotic ulcer at the base of the left fifth metatarsal, and a gangrenous ulceration 4 by 4 by .5 cm. in size on the lateral dorsal portion of the foot. Culture of the purulent exudate revealed hemolytic streptococci and coagulase negative staphylococci. Conservative soft tissue débridement of the connecting dorsal and plantar areas was done, and the patient was given twenty injections of intra-arterial penicillin over thirteen days. The wound was clean and granulating at this time and one week later the plantar area was healed. The dorsal area of defect was then pinch grafted and nine-tenths of the pinch grafts took. The foot was well healed eleven days after the grafting and the patient has been ambulatory and had no further difficulty during the four months since that time.

Comment.—Control of infection in this case of diabetic gangrene made it possible to save the foot and successfully skin graft an area which had previously been gangrenous.

CASE 5.—L. M., a 66-year-old woman, was admitted with generalized arteriosclerosis, terminal renal arteriosclerosis, and wet gangrene of the entire right hallux and two inches of

the dorsal and volar surfaces of the foot. She was known to have had diabetes for twelve years and the presence of severe renal arteriosclerosis and uremia had been determined two and one-half years previously. A progressive infection and gangrene of the right foot had occurred over a three-month period prior to the time she was seen.

Intra-arterial penicillin (50,000 units), papaverine, and potassium permanganate foot soaks were given twice daily for one week with subsidence of infection and demarcation of the area of gangrene. The patient's general condition was terminal, however, so that all surgery was thought to be contraindicated. The patient continued in a semicomatose state but on medical management was still living one month later. A local débridement of the gangrenous toe was then done and this was unfortunately followed by a flare-up in the cellulitis of the foot. Penicillin was given intramuscularly in a dosage of 20,000 units every three hours for six days following the débridement but the cellulitis continued to progress on the foot. Four intra-arterial penicillin injections of 50,000 units each were then given over forty-eight hours and the cellulitis disappeared completely. Unfortunately, however, the patient succumbed to the renal disease shortly thereafter.

Comment.—A severe recurrent cellulitis in an arteriosclerotic diabetic patient was progressing with large doses of intramuscular penicillin for six days but cleared completely with a smaller dosage of penicillin given by the intra-arterial route.

CASE 6.—B. C., a 66-year-old diabetic woman, had an edematous inflamed right foot with a purulent undermining gangrenous ulcer of the lower lateral leg which had enlarged over a six-week period, while the patient was on bed rest, until it was 15 by 12 by 1 cm. in size. The edges of the ulcer were undermined suggesting a Meleney ulcer but initial cultures of the ulcer revealed hemolytic streptococci and coagulase-positive staphylococci. Ten intra-arterial injections of penicillin were given over the course of one week and the base of the ulcer improved. The necrotic overhanging ulcer edges were excised at that time and culture of the necrotic tissue revealed both *Clostridium welchii* and micro-aerophilic streptococci to be present. She was given 20,000 units of penicillin intramuscularly every three hours and five intra-arterial injections over the next three days; the cultures became negative for *Cl. welchii*. However, the patient presented signs of vascular impairment and amputation was decided upon. An incision made into the calf revealed the muscles to be necrotic in spite of the intact overlying skin so a disarticulation was done at the knee. The operative specimen revealed old organized thrombi in both the anterior and posterior tibials and arteriosclerosis and 30 per cent narrowing of the peroneal artery. Subsequently a mid-thigh amputation was done after an intra-arterial injection of penicillin was given preoperatively. A secondary skin closure was done because this was an early case. The stump healed well.

Comment.—Intra-arterial and intramuscular penicillin controlled a *Cl. welchii* and microaerophilic streptococcal infection in the lower leg with both the anterior and posterior tibial arteries completely occluded and a 30 per cent narrowing of the peroneal artery indicating the possibilities of control of infection even in the presence of marked vascular impairment.

CASE 7.—K. K., a 66-year-old diabetic man, had a severe cellulitis and inflammatory edema of the entire left foot and leg extending up to the knee. The infection had progressed over the course of one month while the patient was on bed rest. The dorsum of the great toe had a deep abscess with a draining sinus tract present (Fig. 7). X-ray examination of the foot revealed an osteomyelitis of both phalangeal bones of the great toe, and cultures revealed coagulase-positive staphylococci, hemolytic streptococci, and *Escherichia coli* to be present. He was given two intra-arterial penicillin injections of 50,000 units each and the cellulitis and inflammatory edema disappeared within twenty-four hours. The abscess on the left hallux was then incised and about 2 c.c. of yellow pus were evacuated (Fig. 8). Five additional

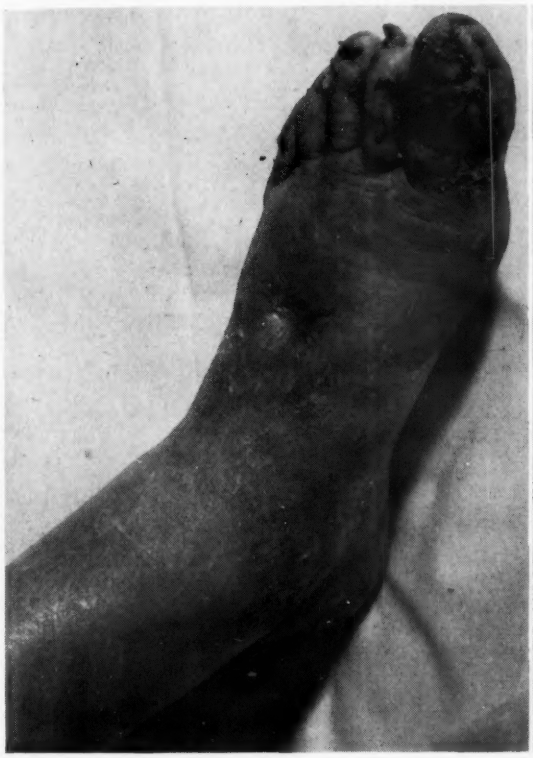


Fig. 7.

Fig. 8.

Fig. 7 (Case 7).—Marked cellulitis and edema of left foot prior to therapy (note pitting edema of dorsum of foot).

Fig. 8 (Case 7).—Left foot after forty-eight hours of therapy, revealing disappearance of cellulitis and edema.

Fig. 9 (Case 7).—Stump of left hallux healed by primary intention of twelfth postoperative day.

intra-arterial injections were given during the following week and portions of necrotic tendons sloughed spontaneously. The toe was then amputated through the proximal phalanx under intra-arterial procaine anesthesia using 25 c.c. of 2 per cent procaine with 50,000 units of penicillin added. After this injection the Dos Santo stasis technique was used in which the cuff was inflated to 280 mm. of mercury and hemostasis was accomplished during the procedure. A primary closure of the amputation stump was done. No pain or discomfort was experienced by the patient during the procedure. Postoperatively the patient was given six routine intra-arterial penicillin injections and the stump healed by primary intention (Fig. 9). Subsequent roentgenograms of the left foot revealed no residual osteomyelitis in the stump of the phalangeal bone of the hallux.

Comment.—The subsidence within twenty-four hours of a severe cellulitis of the leg which extended up to the knee and the subsequent primary healing of an amputation done through an area of osteomyelitis in the toe demonstrates the rapidity and efficacy of intra-arterial penicillin therapy.

CASE 8.—J. P., a 62-year-old nondiabetic woman, had cardiac failure and arteriosclerotic gangrene of both feet. A massive gangrene of the right foot and lower third of the leg was present with cellulitis and edema extending up to the knee. Dry gangrenous areas with surrounding cellulitis were present on the left second and third toes, medial malleolus, and heel. Cultures revealed hemolytic streptococci, coagulase-negative staphylococci, and aerobacter. Six intra-arterial penicillin injections of 50,000 units each were given bilaterally over five days. The cellulitis regressed to a point two-thirds up the right leg after twenty-four hours and no cellulitis was evident on either leg after forty-eight hours. A steady fall in the leucocyte count occurred, from 21,000 to 9,000, over six days of therapy. The gangrenous portions of the toes on the left foot sloughed spontaneously and all infection cleared. A definitive closed right supracondylar amputation was done and the stump healed by primary intention. Pathologic examination of the specimen revealed organized thrombi in all three major arteries of the lower right leg and 90 per cent occlusions of the popliteal artery.

Comment.—Infection in a massive arteriosclerotic gangrene was controlled in spite of the occlusion of all three main arteries of the lower leg and a definitive supracondylar amputation healed by primary intention.

CASE 9.—A. D., a 40-year-old woman, had gangrenous areas due to frostbite on the medial three toes of each foot and both heels, a severe cellulitis of the feet, and systemic toxicity with the temperature elevated to 105.6° F. She was given nine intra-arterial penicillin injections over a period of six days, at which time she was afebrile, the cellulitis had disappeared, and the dry gangrenous areas were demarcating well. A considerable portion of the dry gangrenous areas sloughed spontaneously during the next six days, at the end of which time the patient was given 50,000 units of penicillin in 50 c.c. of 1 per cent procaine into the femoral artery with the blood pressure cuff, which subsequently pumped 280 mm. of mercurcy. Then a removal of the remaining eschar and an amputation of the distal half of the distal phalanx of the second left toe were done painlessly without additional anesthetic agents. Both feet had healed completely one month later.

Comment.—The infectious element was effectively controlled in this case of gangrene due to frostbite and a demarcation of a smaller area of dry gangrene permitted so that only a small local amputation was necessary.

CASE 10.—M. S., a 79-year-old woman, was admitted with diabetic arteriosclerotic gangrene of both feet. There was a wet gangrene of the right second toe and 2 cm. of the adjacent foot, and a dry gangrene of the distal one-fourth of the left second toe. A culture of the right foot revealed gram-positive cocci, *Esch. coli,* Proteus, and Aerobacter. Roentgenograms revealed calcification of the arteries of the foot, osteomyelitis of the right second middle

and proximal phalanges, and left second proximal phalanx. A routine regimen of intra-arterial penicillin (50,000 Oxford units), papaverine, and potassium permanganate foot soaks (1:9000 concentration) was given bilaterally twice daily for a total of fourteen injections. The area of wet gangrene on the foot regressed, and an amputation of the second right toe was then done through the area of osteomyelitis in the proximal phalanx. This site was chosen to determine whether or not the penicillin had eradicated the bone infection. The wound was closed secondarily twelve days later since this was an early case, and the full benefits of the therapy were not yet appreciated. Healing was slow but complete in less than two weeks. The gangrenous portion on the second left toe sloughed spontaneously, and the toe healed completely with a small scar prior to discharge. A recheck x-ray examination of the right foot, two months later, revealed no evidence of osteomyelitis in the amputated stump of the proximal phalanx. During the more than one-half year since hospital discharge, the patient has been ambulatory and has had no further difficulty.

Comment.—Complete arrest of infection by intra-arterial penicillin has permitted the site of a right second toe amputation for gangrene to remain healed for over one-half year although the amputation was done through an area of osteomyelitis, the foot had been involved by wet gangrene, and the interdigital arteries of the foot were revealed by roentgenogram to be calcified.

CASE 11.—R. A., a 19-year-old man, developed a postoperative infection of the left knee joint following the operative removal of a torn anterior cruciate ligament and medial meniscus. The septic course followed subsequently is shown in Fig. 10. Cultures of the purulent exudate revealed coagulase-positive staphylococci to be present. Multiple therapeutic measures including three courses of high dosages of intramuscular penicillin, and one course of oral sulfadiazine, gave no beneficial results over a period of seven weeks. However, sensitivity tests on the strain of staphylococcus present in the pus at this time revealed the organism to be inhibited by a penicillin concentration (Pfizer 125) of .8 units per cubic centimeter. Intra-arterial penicillin was started at this time and twelve injections were given over nine days. The severe suppurative arthritis healed completely in eighteen days. Physiotherapy started two weeks after this time resulted in no flare-up of the infection and the patient was able to flex the knee 20 degrees prior to hospital discharge.

Comment.—The failure of high dosages of intramuscular penicillin is attributed to the tissue barriers of the knee which excluded local permeation of the drug and prevented success although the *Staph. aureus* present was susceptible to penicillin as shown in sensitivity tests. Intra-arterial administration of penicillin overcame this tissue barrier and made control of the infection possible.

CASE 12.—A. E., a 63-year-old diabetic man, had moderate arteriosclerotic cellulitis of the dorsum of the foot and a painful perforating infected ulcer on the sole of the left foot of three months' duration. Culture of the purulent exudate revealed coagulase-positive staphylococci and aerobacter. An area of callus surrounding this ulcer was excised and potassium permanganate foot soaks, papaverine, and intra-arterial penicillin were given twice daily for five days. The cellulitis on the dorsum of the foot disappeared in two days, and the ulcer healed in one week, but the patient was not allowed to bear weight on the foot for two weeks. In the four months since that time the patient has been able to walk on the foot without pain or recurrent ulceration.

Comment.—Diabetic perforating ulcer of the sole of the foot usually resistant to therapy healed rapidly on intra-arterial penicillin therapy.

CASE 13.—I. S., a 32-year-old woman, had an enlargement of the entire left leg secondary to an old thrombophlebitis, large superficial varices, and a chronic deep ulceration

over the left medial malleolus with hemolytic streptococci present. A venogram revealed a thrombosis of the saphenous vein in the lower leg adjacent to the ulceration, but a patent deep circulation. Three intra-arterial injections of 50,000 units each were given during the forty-eight hours prior to surgery and then 200,000 units of penicillin injected down the saphenous vein; a high saphenous ligation and an excision of the ulcer were done under spinal anesthesia. A split-thickness skin graft placed over the ulcer on the sixth day had a 95 per cent take.

Comment.—Successful skin grafting of a chronic thrombophlebitic ulcer with hemolytic streptococcal infection was facilitated by proper penicillin therapy.

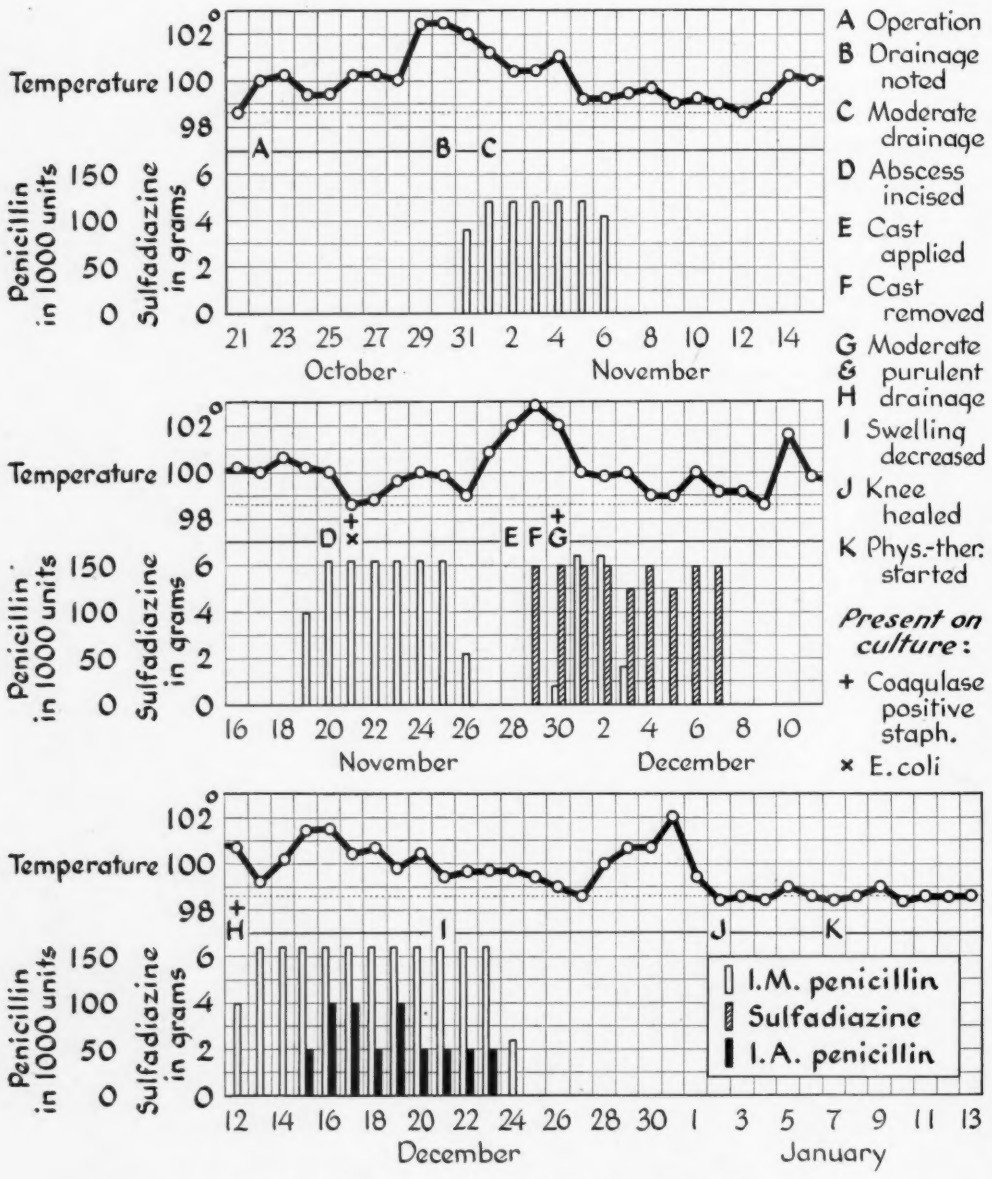


Fig. 10 (Case 11).—Course during hospitalization.

CASE 14.—J. D., an 18-year-old girl, with a proved diagnosis of acrocyanosis had previously had sympathectomies on all four extremities. In spite of this a necrotic ulceration had developed on the first and second left toes at a site of infection and had been unresponsive to various local medicaments tried over a two-week period. Neither the dorsalis pedis nor the posterior tibial artery of the foot was palpable. Culture of the pus revealed hemolytic streptococci and coagulase-negative staphylococci to be present. The ulcer was débrided and two intra-arterial injections of penicillin were given, resulting in a disappearance of the infection within three days.

Comment.—Intra-arterial penicillin effectively cleared the infection in a foot ulcer in a patient with acrocyanosis in spite of the impaired blood supply to the area.

CASE 15.—F. H., a 45-year-old man, had a cellulitis, paronychia, and subungual abscess of the right thumb. Temperature was 100.8° F. and the pulse 110. The leucocyte count was elevated to 14,500. He was started on full therapeutic doses of sulfadiazine (1 Gm. every four hours) and drainage of the abscess was effected by incision and removal of the radial third of the thumbnail. Temperature returned to normal within twenty-four hours but three days later an erythema of the distal two-thirds of the distal phalanx with marked tenderness of the center of the palmar aspect indicative of an infection of the distal closed space of the thumb (felon) developed. Sulfadiazine was stopped and the patient was given one injection of 50,000 units of penicillin into the right brachial artery. Within forty-eight hours all inflammation and tenderness were controlled without incision of the felon. The patient had no further difficulty with the thumb.

Comment.—A felon which developed while the patient was on sulfadiazine therapy cleared completely in forty-eight hours without incision after one intra-arterial injection of penicillin (50,000 units).

CASE 16.—A. K., a 32-year-old physician, developed an infection of the left index finger and a tubular lymphangitis of the arm a few hours after he had accidentally pricked himself while operating on a patient with gas gangrene and hemolytic streptococcus cellulitis of the abdominal wall. Within twelve hours the temperature was elevated to 103° F. and the condition was toxic. He was then given 50,000 units of penicillin intra-arterially into the left axillary artery. Twelve hours later the cellulitis was receding, but intramuscular penicillin was started (20,000 units every three hours) as an additional precautionary measure. Local inflammation had disappeared by thirty-six hours and he was afebrile by forty-eight hours. However, the patient from whom he had contracted the infection died of a fulminating gas gangrene of the abdominal wall in spite of intramuscular penicillin therapy and additional measures. The physician left the hospital in four days with no residuals.

Comment.—Rapid control of an acute fulminating infection of an arm was possible by intra-arterial and intramuscular penicillin in this case.

CASE 17.—A. G., a 70-year-old diabetic woman, had developed a severe postoperative infection following a bunion operation done elsewhere. A severe osteomyelitis and cellulitis progressed in spite of therapy and the patient was referred for amputation two months later. Physical examination at this time revealed a purulent draining operative incision with surrounding ulceration of the skin of the medial side of the foot and a cellulitis of the dorsum of the foot. Roentgenogram of the foot revealed a severe osteomyelitis at the operative site (Fig. 11). Intra-arterial penicillin, papaverine, and potassium permanganate foot soaks were given twice daily and all cellulitis disappeared in forty-eight hours. All drainage ceased by the sixth day. Intra-arterial penicillin was continued, however, until thirty injections had been given. The epithelium grew in well, and six weeks after the start of the therapy the skin had epithelized over the area. The patient has walked on the foot for five months

since then with no pain or signs of recurrent infection. Roentgenogram of the foot at this time revealed a good bony union at the operative site with no evidence of osteomyelitis (Fig. 12).

Comment.—A severe wound infection, cellulitis, and osteomyelitis following a bunion operation responded well to intra-arterial penicillin.

Fig. 11. Fig. 12.

Fig. 11 (Case 17).—X-ray of right foot revealing marked osteomyelitis present at first metatarsophalangeal junction with soft tissue swelling of foot.

Fig. 12 (Case 17).—X-ray revealing good bony union with no evidence of osteomyelitis five months after hospital discharge.

Discussion of Possible Objections and Contraindications to the Technique.—Because of the frequency with which veins are used for infusions rather than arteries, there may be a natural antipathy on the part of the clinician toward arterial puncture. This misconception has no basis in fact, since the distributing arteries are usually much more suitable anatomically than their concomitant veins for repeated puncture. Thus, in the histology by Maximov and Bloom,[21] we note that, "The wall of the veins is always thinner, softer, and less elastic than that of the arteries." The better development of muscular and elastic tissue in arteries as opposed to the greater prominence of connective tissue in the veins is also mentioned. In the arteries, the internal elastic membrane adjacent to the tunica intima is very well developed and acts as an efficient self-sealing mechanism. Evidence of this efficiency can be deduced from Case 17 in which a 70-year-old woman received a total of thirty intra-arterial injections at approximately the same site in the common femoral artery over a period of sixteen days without hematoma formation or any other difficulty. Similarly, there has been no incidence of hematoma formation in any of the other patients treated.

Regarding the selection of drugs for intra-arterial injection, Huet and Bargeton[22] and Wilmoth[23] demonstrated in experimental animals that solutions approaching the isotonicity and pH of the blood were the safest to use. The same is true for intravenous medications, but to a lesser extent. In intra-arterial injections, the factor of hemodilution is less, and the more concentrated solution comes in contact with the capillary endothelium almost immediately. Dos Santos[5] noted the occasional vasomotor phenomenon of arterial or venous spasm in the upper extremities but rarely in the lower extremities. These episodes were readily relieved by a procaine block of the sympathetic ganglia. He has never noted an arterial thrombosis, and no thromboses were seen in any of the present series.

Regarding possible contraindications to intra-arterial therapy, Luccarelli[12] stated that the method is contraindicated in diabetes, arterial incompetence, hypotension, and nephritis, but no explanation is given. However, a large portion of the cases in the present group had diabetes and arterial incompetence, and these were among the most impressive results. Glasser and co-workers[16] gave thrombophlebitis as a contraindication, but in those cases in which infection plays an important part, as evidenced by erythema and increased warmth, intra-arterial penicillin gives good results. It is thought advisable, however, always to supplement intra-arterial injections in these cases with sympathetic blocks, as a prophylactic measure against increased vasospasm. In those cases, in which stasis is thought to be a more prominent factor as evidenced by a cold swollen extremity intra-arterial penicillin should not be used, as the benefit will be minimal since infection has only a minor role. This, together with the presence of a locally infected area over the site of injection, is the only contraindication to this mode of therapy of infections of the extremities.

SUMMARY

1. Intra-arterial penicillin effectively overcomes the difficulties offered by tissue barriers and vascular impairment in infections of the extremities which reduce the efficacy of penicillin administered intravenously or intramuscularly.

2. The technique of injection is simple and safe and has not been followed by complications in any of the forty patients treated.

3. The only contraindications to the method are phlebothromboses or a locally infected area over the site of injection.

4. The method effectively controls various types of infections of the extremities with and without tissue necrosis so that surgery is obviated and simplified in many cases, and in others it is changed from an emergency status to an elective procedure making possible a better evaluation and preoperative preparation of the patient.

5. Intra-arterial procaine given together with the penicillin is also presented as an efficient method for simple local surgery of the extremities, whereby anesthesia, hemostasis, and chemotherapy are all obtained by a single procedure.

6. Intra-arterial penicillin is more rapid in its effect than penicillin administered by the usual means.

REFERENCES

1. Heddaus, H.: Beitrage zur Heilserumbehandlung des Tetanus, München. med. Wchnschr. **61**: 2186, 1914.
2. Goyanes, J.: Tratamiento Quimioterapice, Par la via Arterial, de las Tuberculosis locales, Rev. clín. de Madrid **12**: 261, 1914.
3. Fiolle, Jean, and Fiolle, Paul: Essais d'hematose artificielle et d'angeio therapie artérielle, Marseille-méd. **16**: 597, 1914.
4. Dos Santos, R.: L'artériographie de l'abdomen et des membres et les horizons de la voie artérielle, Med. contemp. **47**: 141, 1929.
5. Dos Santos, R.: Arterial Injections With Stasis in the Therapy of Infections, SURGERY **5**: 436-443, 1939.
6. Lamas, A.: Therapeutique par voie artérielle, Cong. franç. de chir. **42**: 384, 1933.
7. De Fourmestraux, J.: La voie artérielle dans le traitement du tétanos, Mém. Acad. de chir. **63**: 550, 1937.
8. Fredet, M.: Les infections intra-artérielles de mercurochrome dans le traitment des infections de membres des plaies atones et des ulceres variqueux, Cong. franç. de chir. **46**: 543, 1937.
9. Leriche, R.: A propos de la thérapeutique des infections par voie intra-artérielle, Mém. Acad. de chir. **66**: 47, 1940.
10. Fritzsche, E.: Beitrag zur intraarteriellen Serumbehandlung des Tetanus, Chirurg **8**: 450, 1936.
11. Demel, R., and Sgalitzer, M.: Die therapeutischen Ergebnisse der Arteriographie an den Extremitäten, Wien. klin. Wchnschr. **46**: 1017, 1043, 1933.
12. Luccarelli, V.: Le iniezioni endoarteriose nelle Infezione degli arti, Policlinico (sez. prat.) **42**: 2255, 1935.
13. Martinoff, D.: Intra-arterial Injection of Antiseptic Drugs, Khirurgiya **5**: 22, 1943.
14. Titelbaum, A., and Titelbaum, E.: Intra-arterial Introduction of Drugs for Treatment of Local Inflammatory Processes of the Extremities, Khirurgiya **2**: 17, 1943.
15. Ribeiro, E. Brancho: Penicilina por via arterial, An. paulist. de med. e. cir. **48**: 93-94, 1944.
16. Glasser, S. T., Herrlin, J. J., and Pollack, B.: Intra-arterial Injection of Penicillin for Infections of the Extremities, J. A. M. A. **128**: 796-802, 1945.
17. Lewis, Thomas, and Grant, R. T.: Observations on Reactive Hyperemia in Man, Heart **12**: 73, 1925.
18. Lewis, Thomas: The Tone Exerted by the Minute Vessels of the Skin in Contracting, Heart **11**: 109, 1924.
19. Pillsburg, D. M., Sulzberger, M. D., and Lwingood, C. S.: Manual of Dermatology, Washington, D. C., 1943, National Research Council, p. 201-219.
20. Babcock, Wayne W.: Deodorants, J. A. M. A. **129**: 1094-1095, 1945.
21. Maximov, A. A., and Bloom, W.: A Textbook of Histology, ed. 3, Philadelphia, 1939, W. B. Saunders Company, p. 242.
22. Huet, P., and Bargeton, D.: Sur quelques effets des injection intra-arterielle, Presse méd. **44**: 677, 1936.
23. Wilmoth, P.: Treatment by Intra-Arterial Injection, Presse méd. **47**: 1249, 1939.
24. Varco, R. L.: The Preoperative Dietary Management for Surgical Patients With Special Reference to Lesions of the Stomach and Duodenum, SURGERY **19**: 303-378, 1946.
25. McAdam, I. W. J.: Penicillin Treatment of Acute Hematogenous Osteomyelitis, Brit. J. Surg. **33**: 167-172, 1945.

THE IMPORTANCE OF PRECISE BACTERIOLOGIC DATA IN THE TREATMENT OF INFECTIONS OF THE UROGENITAL TRACT

JOSEPH A. LAZARUS, M.D., AND LEWIS H. SCHWARZ, B.S., NEW YORK, N. Y.

GREAT strides have been made in the diagnosis and treatment of diseases of the urogenital tract within the past ten years. It seems to us, however, that we are now entering an era when even greater advances will be made in treating urinary tract infections, because of phenomenal discoveries in the fields of antibiosis and chemotherapy.

Until recently the treatment of urinary tract infections has been more or less haphazard and empirical, primarily because of (1) failure to identify causative organisms of infections; (2) nonavailability of, or failure to use, drugs capable of destroying offending organisms; and, finally, (3) failure to relieve concomitant obstructions impairing free urinary drainage.

A fully equipped bacteriologic laboratory staffed by a competent bacteriologist, especially as it pertains to the treatment of infectious uropathies, has become an indispensable accessory in the practice of modern urology. The time has passed when urologists were willing to accept reports from laboratories giving group designations of organisms instead of specific identifications. To state, for example, that a sterilely obtained specimen of urine shows a growth of *Bacillus pyocyaneus,* without testing its behavior in vitro, can result in a false conception regarding pathogenicity and, at times, lead to dire results because of inadequate treatment.

A patient (Mr. J. P.) was operated upon by the senior author (March, 1940). A right nephrectomy and subtotal ureterectomy were performed for suppurative pyelonephritis, ureteritis, and multiple renal calculi. During the course of a routine follow-up urologic examination (April 9, 1946), a gram-negative encapsulated rod was discovered on culture in the bladder urine specimen. Urine from the left kidney was negative on smear and sterile on culture. The colony appeared mucoid, was distinctive because of its heaped-up character, and was distinctly hemolytic. Although the organism presented close similarity to the Friedländer bacillus, we deemed it advisable to carry out further studies. When inoculated into Kligler's iron agar, it became immediately evident that we were not dealing with a Friedländer bacillus because of the negative butt and slant, indicating lack of acid and gas formation. Following inoculation of routine differential media the organism was ascertained to be a mucoid variant of *Pseudomonas aeruginosa* (*B. pyocyaneus*). Due to the similarity of this organism to *Pseudomonas fluorescens,* differentiation could be made only by establishing the pathogenicity through animal inoculations. In vivo studies readily disclosed that we were dealing with a virulent organism of great toxicity which promptly killed all animals used in the examination. A careful assay was then carried out which disclosed that the growth of this or-

Received for publication, June 26, 1946.

ganism was inhibited by streptomycin, but was in no way influenced by penicillin or the sulfonamides.

For several years reports have been received, in which the causal organism was called *Staphylococcus albus* until one of us (L. H. S.) began the routine use of differential media as a means of specific identification of bacteria. We were surprised to find that what on casual inspection appeared to be a *Staph. albus* was actually a *Staph. aureus.* The reason for this error was that colonies of *Staph. aureus* grown on agar plates frequently appear white on mere inspection. Careful scrutiny of these colonies, however, usually discloses a faint yellowish tint. The exact nature of the bacterium is readily ascertained from its behavior on differential media.

One of the most common organisms apparently isolated in the urine is the *Bacillus coli,* with no further descriptive elaboration from the bacteriologist. Yet, the designation *B. coli* is indefinite because of the multiplicity of organisms constituting this group. Most bacteriologists plate specimens on eosin-methylene blue, agar, with the result that any colony which presents a metallic sheen is classified in the group of *B. coli.* It should be recalled, however, that any organism which ferments lactose will form this variety of colony when grown on this agar. The two groups of organisms falling within this category are aerobacter and escherichia. The former, which comprises such organisms as (1) *Aerobacter aerogenes,* (2) *Aerobacter cloacae;* and (3) *Aerobacter sp.* (an heterogeneous group), should not be classified as *B. coli* because the latter group, which consists of *Escherichia coli* (communis and communior) and *Escherichia freundii,* constitute the true members of the *B. coli* category. Although members of both categories may invade the urogenital tract and cause great pathologic changes, the first is usually associated with the gastrointestinal tract, while the second is a common cause in infections of the urinary tract. As a rule both groups are readily destroyed by the sulfonamides and by streptomycin, but are unaffected by penicillin.

For several years the subject of amicrobic pyuria has been discussed in medical literature. We are all undoubtedly aware that a sterilely obtained specimen of urine containing leucocytes, which fails to show organisms on smears, must be carefully examined for the mycobacterium of tuberculosis, especially in acid urines. The absence of this organism and failure to obtain a growth on the commonly employed aerobic culture media has led observers to group such examples in this category. It seems to us, however, that before doing this, specimens should be cultured on carefully selected anaerobic media. There are approximately twelve anaerobic organisms, ranging from micrococci to the gram-negative nonspore-forming rods, and including one member of the Neisserian group, which are obligate anaerobes showing pathogenic features when invading the genitourinary tract. It is our routine to use anaerobic media whenever urines fail to show organisms upon routine aerobic media, and upon all urines obtained from patients who present symptoms suggestive of urinary tract infection regardless of the presence of cellular elements in the urine. We have in mind supplementary reports regarding this subject to be published in the near future.

PROCEDURES

The Procurement of Sterile Specimens of Urine.—Careful bacteriologic studies necessarily depend upon the manner in which specimens of urine are obtained from patients. It is obviously futile to expect accurate culture data from specimens contaminated before reaching the laboratory, or inadvertently sterilized at the source or during transit to the laboratory. All specimens obtained from women should be catheterized, using sterile catheters which are aseptically introduced after carefully cleansing the urethral meatus. A further precaution against contamination is to allow the first few cubic centimeters of urine to escape before collecting the specimen in a sterile container. In men the meatus should also be carefully cleansed before permitting them to void or immediately prior to catheterization or cystoscopy, and, as in the case of women, the first few cubic centimeters of urine should be discarded before the specimen is collected.

The collection of specimens for culture from the renal pelves through ureteral catheters must be done with great circumspection in order to avoid contamination or sterilization from the use of strong disinfectants. A frequent practice is to sterilize the ends of the catheters, following catheterization of the renal pelves, with a disinfectant such as bichloride of mercury, and then to introduce the catheter ends into sterilized test tubes which are promptly stoppered by means of sterile cotton plugs around the catheters. This technique may, at times, result in sterile cultures because a few drops of the disinfectant which may be too concentrated is accidentally permitted to drip into the test tubes. To avoid this, it is advisable, when a disinfectant is used, that it be diluted and applied to the ends of the catheters on pledgets of cotton which have been squeezed dry in order to avoid dripping into the test tubes. A far better practice is to avoid the use of disinfectants entirely and to depend on keeping the ends of the ureteral catheters sterile during the entire cystoscopic procedure. For several years one of us (J. A. L.) has routinely used small lengths of sterilized pipettes which are sealed at one end and capped at the other end with a perforated rubber nipple through which the end of the catheter passes for a distance of two to three inches. The pipette, being snugly fitted over the end of the catheter, cannot become dislodged during the course of the cystoscopic manipulation. Following the introduction of the catheters into the renal pelves, the pipettes are removed and the untouched ends of the catheters are immediately placed in sterile test tubes which are promptly stoppered with sterile pledgets of nonabsorbent cotton applied firmly in order to prevent dislodgment of the catheters while collecting the specimens.

Failure to use careful aseptic technique during the course of cystoscopies will obviously defeat all subsequent attempts to obtain accurate bacteriologic data. This requires constant vigilance on the part of the urologist, not only regarding the cystoscopic procedure, but in maintaining absolute sterility of cystoscopes, catheters, and other necessary equipment. To accomplish this end, frequent periodic testing of supplies and equipment by strict bacteriologic methods is required.

Laboratory Procedures.—Upon examination of specimens, urine specimens, preferably freshly procured, should be collected into two tubes, one for smears and the other for culture. Negative smears of a thoroughly centrifuged urine specimen do not necessarily, as aforesaid, indicate absence of bacteria. We have repeatedly found this to be the case, and contrary to what has frequently been advocated, we routinely culture all urines, regardless of the results of the smears. Failure to follow this procedure and to rely upon smear diagnoses, that is, making gram stains of smears taken from growths on culture media, often leads to errors in diagnosis. For example, an orange-yellow colony is frequently seen on plates, which upon the stained smear discloses cocci in small clumps. Failure to employ differential media may lead to calling this *Staph. aureus*, whereas if it were run through the media it would be found to be *Micrococcus aurantiacus*. In the same manner, *Micrococcus cereus* may be mistaken for *Staph. albus*, except that the former does not liquefy gelatin. All of these organisms are pathogens and have been isolated from foci of infections, yet not all of them respond similarly to chemotherapy. It is, therefore, important that differential media be used, as well as that chemotherapeutic assays be run in order to ascertain the sensitivity of bacteria to drugs.

When urines are inoculated into broth media, it is frequently found that in the presence of a multiplicity of organisms the bacteria showing the most luxuriant growth propensity completely overgrow all others, making it impossible on the subsequently transplanted agar plates to isolate and thereby identify the various bacterial colonies present. For this reason we have found it advantageous immediately to streak blood agar plates at the same time that the broth media are inoculated. Differential media and in vitro examinations are made routinely.

Whenever an organism is isolated which fails to conform to the usual standards, animals are inoculated and further examinations made. Only in this way can the bacteriologist determine the behavior and pathogenicity of the unusual causal organism. Careful assays must be made occasionally in order to ascertain the toxicity of bacteria, as well as the effect that specific therapy may exert upon them. A common method used by laboratories in order to ascertain pathogenic tendencies of bacteria is to determine the capacity of the organism to hemolyze blood agar. Yet, it is common knowledge that many saprophytes also show this tendency by virtue of their ability to hemolyze blood through metabolic processes. On the other hand, it is also known that many pathogens fail to show this tendency. Animal inoculation is the only certain method of determining the degree of pathogenicity of bacteria.

Adaptation of Drug to Organism.—With specific therapeutic agents becoming available in ever-increasing numbers, it becomes necessary for the urologist to ascertain, whenever treating infections of the urogenital tract, not only the adaptability of antibiotics to the nature of offending organisms, but also the correct dosages required to achieve adequate results. The tendency to rely on instructions furnished by drug manufacturers in the use of chemotherapeutic agents or on the opinions of writers in their various publications is not devoid

of risks because of the general tendency of dealing with (1) group classification of bacteria, and (2) the effect of given drugs on organisms of average virulence.

It is common knowledge that variations in virulency and behavior toward chemotherapeutic agents frequently occur among organisms belonging to the same group of bacteria, so that the validity of what has been generally established as optimum dosage to promote bacteriostasis or a complete bacteriocidal effect of a given drug on a certain group of organisms is open to question. The only consistent way of ascertaining the most efficacious drug and its optimum dosage is to carry out careful assays on all urine specimens whenever an infection is due to an organism which shows any striking variations from the normal behavior of bacteria belonging to that group, but which does not respond to the usual chemotherapeutic agents recommended for its destruction. In this way alone is it possible to ascertain (a) whether a given drug is capable of destroying the causal bacteria, and also (b) the optimum dosage of the drug in order to accomplish a cure.

Establishing Efficacy of Therapy.—To establish the effectiveness of a drug in the treatment of any infection of the urogenital tract, it is well to recall certain well-established criteria, namely: (1) Has the drug resulted in the complete abatement of symptoms and physical signs of infection? (2) Has the administration of the drug resulted in permanent destruction of the causal bacteria? Although it would seem that full realization of the first criterion would also result in the accomplishment of the second, this does not hold true in routine practice. The fact that a patient is symptom-free, shows no cellular elements in the urine, and discloses no cystoscopic evidence of persistent infection, does not necessarily indicate that the causal organism has been destroyed. This can be established only after periodic culture studies of the urine, which may take weeks or months to accomplish. This is especially true now with the availability of specific chemotherapeutic drugs and their injudicious and promiscuous use regarding selectivity and especially dosage. This tendency is invariably noted in the case of sulfonamides, and is now being witnessed with like frequency in the use of penicillin. The reason for this, as it appears to us, is that the improper selection and administration of a chemotherapeutic drug will in no way interfere with the growth or pathogenicity of an organism. Likewise, the use of such a drug in insufficient dosage, by promoting incomplete bacteriostasis, temporarily retards the growth of the bacteria on the usual culture media. This does not signify that the organism has been killed or made permanently innocuous; it simply means a temporary retardation of the bacteria's propensity to growth on the usual media. Given time and favorable circumstances, such as lowering of a patient's resistance, the organism will promptly assume its former state of pathogenicity. It is for this reason that frequent follow-up cultures are indispensable in determining the efficacy of any drug in the treatment of infectious uropathies by chemotherapeutic agents.

Dangers Attendant on the Indiscriminate Use of Modern Chemotherapeutic Drugs.—Urologists will readily attest to the almost daily experience of having patients state that in the course of treatment they have been given sulfonamides

or penicillin by their physicians long before they have been subjected to urologic examinations and before any attempt was made to identify the causal organism of infection. We have received innumerable requests from patients as well as physicians for information regarding the use of drugs which would cure urinary infections. They are frequently surprised when asked whether the urine has been cultured, stating that they believed this to be an unnecessary procedure in view of the availability of such "wonder drugs" as sulfonamides, penicillin, and especially the "mysterious superdrug" streptomycin, glowing accounts of which they read in newspapers or medical periodicals. It makes little difference to the average physician, when using penicillin, whether the organism is a member of the *B. coli* group or a virulent strain of pyocyaneus or *Bacillus proteus,* little realizing that these organism are not affected by this drug. But the outstanding risk of the indiscriminate use of chemotherapeutic drugs is not so much the deleterious effects which they may have on the patient, but rather the dangerous effects of the drugs in provoking a state of resistance by the patient to the particular drug, so that should subsequent circumstances make it exigent to use drugs against an organism known to be susceptible to them, their potency will be greatly nullified by the induced resistance of the patient.

Likewise, if correctly selected drugs within this category are used in insufficient dosages, organisms may readily develop an immunity to them, so that within a short time they are no longer inhibited. In other words, a good rule to follow when using antibiotics is to select a drug that is known to be specific for causal bacteria and to use it in sufficient dosage to destroy them promptly and permanently.

SUMMARY AND CONCLUSIONS

With the advent of chemotherapy, the treatment of urogenital infections has become completely dependent on the bacteriologic laboratory. We can no longer remain indifferent to the causative organism when treating infections. Urologists must insist upon precise identification of bacteria rather than upon group designations, because members of the same species of bacteria may show decided variations in pathogenicity and reactivity to drugs generally considered specific for the species. This requires constant access to a well-equipped laboratory and the work of a competent bacteriologist who is capable of carrying out in vitro and in vivo studies of bacteria, as well as accurate assays on the toxicity of organisms, their reaction to drugs, and the most effective dosages required to exterminate them.

To avoid contaminating urine specimens, careful attention must be paid to maintaining asepsis in obtaining specimens from the bladder and kidneys. The use of strong antiseptics capable of sterilizing urines at the source and during transport must be circumspectly avoided.

We have attempted to outline the routine used in our laboratory of obtaining and examining urine specimens, with the view of showing the need of bacteriologic laboratory facilities as essential features in the office armamentarium of the urologist. The prompt and frequent culture examinations of freshly procured urine specimens, without subjecting patients to financial

hardships, can be attained only by making the urologist completely independent of hospital or commercial laboratories.

Since success in treating urologic infections is dependent on drugs accurately selected regarding their ability to eradicate specific bacteria, as well as on proper dosage, it seems to us that a competent bacteriologist working in close collaboration with the urologist can be of inestimable value in establishing these pertinent data, especially in refractory conditions. The relief of symptoms and the disappearance of physical signs cannot be used as criteria of cure in these conditions. A patient may be considered cured of an infectious uropathy only when bacteria causing the infection have been completely eradicated and this can only be ascertained by periodic bacteriologic examinations of the urine, because of the frequent tendency of modern chemotherapeutic drugs to exert bacteriostatic rather than bacteriocidal effects.

The importance of carrying out anaerobic culture studies in conditions failing to disclose organisms on the usual aerobic media has been stressed. It is our opinion that in many instances of so-called amicrobic pyuria positive cultures will be obtained on anaerobic media.

An attempt has also been made to point out the hazards inherent in the indiscriminate use of chemotherapeutic agents administered in inadequate dosages in the treatment of urologic infections. The principal risks are: (1) establishing resistance of patients to a drug, thereby making the drug ineffective for subsequent use; and (2) establishing resistance by bacteria for a drug especially when it is used in insufficient dosage.

It is manifest to us that better results in handling urinary infections will be attained when urologists include fully equipped bacteriologic laboratories and the services of competent bacteriologists in their office armamentarium. By establishing complete independence of his own laboratory facilities, the urologist will be less apt to assume an indifferent attitude toward the exact nature of the causal bacteria in all infections, and he will also be more certain of obtaining permanent cures.

THE POSTGASTRECTOMY SYNDROME

DAVID ADLERSBERG, M.D., AND ERNST HAMMERSCHLAG, M.D., NEW YORK, N. Y.
(From the Nutrition Clinic and the Medical Services of The Mount Sinai Hospital)

SUBTOTAL gastrectomy is considered to be the method of choice for surgical treatment of peptic ulcer. Jejunal ulcer is an occasional postoperative complication of this operation, whereas it is exceedingly common after gastroenterostomy. A group of patients, however, present a variety of complaints and symptoms after gastric resection even though they do not have peptic jejunal ulcers. This clinical observation is confirmed by comprehensive follow-up studies. In a group of ninety-four partially gastrectomized patients, studied by Sarah Jordan,[1] twenty-seven (29 per cent) had difficulties in maintaining normal weight and presented a definite nutritional problem. Mateer[2] estimated that approximately 14 per cent of his patients showed postprandial symptoms. Miller[3] found in 17 of 240 cases symptoms of weakness, pallor, and loss of weight. Custer, Butt, and Waugh[4] encountered in 28 of 200 cases postprandial symptoms; in twelve cases these symptoms were mild, in ten they were severe and interfered with the daily work of the patients, and the six remaining patients were classified as "gastric cripples" because of their complete inability to work. Berkman and Heck[5] studied extensively the postprandial distress after gastric resection, the so-called dumping syndrome. The distress was more severe in the first two months after the operation than at a later period. In some instances aversion to food developed, the eating habits deteriorated, and this resulted in the consumption of only minimal amounts of food. Sandweiss and associates[6] agreed with Crohn[7] and others, that gastric resection is at present the operation of choice for peptic ulcer but emphasized the importance of postoperative gastrointestinal symptoms without marginal ulcer. In their opinion some of the patients are more incapacitated than those who have recurrent ulcers. Although the number of these patients is fortunately comparataively small, a careful study of their symptoms and signs would appear to be well justified.

During the past three years a group of fourteen patients who underwent subtotal gastric resection was studied at the Nutrition Clinic of Mount Sinai Hospital. All fourteen patients were markedly underweight and were referred to the clinic as nutritional problems. After a thorough clinical examination including x-ray studies and laboratory analyses, various types of high caloric, high protein, high vitamin diets were given, as well as vitamin concentrates and liver extract. The therapeutic results, however, remained, as a rule, unsatisfactory. During the course of the observations a study of the underlying causes of the postgastrectomy syndrome was carried out in each case.

GENERAL CHARACTERISTICS

The group includes thirteen patients with subtotal gastrectomy for peptic ulcer and one case of total gastrectomy for gastric syphilis. Of the thirteen ulcer cases, ten patients had had preoperatively duodenal ulcer and only three a gastric ulcer. Patients who had had resections for carcinoma of the stomach

Received for publication, June 19, 1946.

TABLE I. AGE AND WEIGHT AT ONSET OF ULCER SYMPTOMS, AT TIME OF OPERATION AND AT TIME OF THIS STUDY

NO.	NAME	SEX	AGE (IN YR.)			WEIGHT IN POUNDS			OPERATION FOR GASTRIC OR DUODENAL ULCER
			AT ONSET OF ULCER SYMPTOMS	AT TIME OF OPERATION	AT PRESENT	AT ONSET OF ULCER SYMPTOMS	AT TIME OF OPERATION	AT PRESENT	
1	C. M.	F	26	29	32	130	116	111½	D.U.
2	G. S.	F	25	47	49	114	118	90	D.U.
3	L. Z.	F	16	30	43	130	125	118¾	D.U.
4	J. K.	M	44	45	52	155	120	112	D.U.
5	M. C.	M	27	49	52	120	112	99	D.U.
6	S. R.	M	31	49	52		155	132	D.U.
7	S. Z.	M	53	55	57		158	128	G.U.
8	B. E.	F	34	46	59			95	G.U.
9	B. B.	M	45	49	59	130	111	115½	D.U.
10	L. R.	M	43	43	59	150		125	D.U.
11	F. M.	M	37	53	54	190	162	166	G.U.
12	R. B.	F	16	40	61	132		117	D.U.
13	A. F.	M	15	50	51	178	147½	131	D.U.
14	O. S.	F	?	33	36	114	70	92½	G. syphilis

were purposely not included in this study, since underweight and malnutrition in these individuals may be easily caused by an (undiagnosed) recurrence of the original disease.

Eight of the patients were men, six women. The age at the time of the study varied between 32 and 61 years, the average being 51 years. The comparatively high average age of the group indicates that these patients had been suffering from symptoms of the disease for many years prior to the operation. The age at the onset of ulcer symptoms varied in thirteen patients suffering from peptic ulcer from 15 to 53 years, the average being 31 years. The age at operation varied from 29 to 55 years, the average being 44 years. In other words, the average age at which these patients experienced the first ulcer symptoms was 31 years, at which subtotal gastrectomy had been performed was 44 years, and they averaged 51 years at the time of the study.

The body weight before the onset of symptoms ranged in eleven patients whose statements were reliable between 114 and 190 pounds (average 142.6 pounds), the weight before operation from 70 to 162 pounds (average 126.7 pounds) and at the time of the study from 90 to 166 pounds (average 116.6 pounds). The average patient of this group had lost 15.9 pounds before the operation and, in addition, 10.1 pounds after the operation, the total loss of weight being 26 pounds (see Table I). It is evident that we were dealing with a group of markedly underweight individuals whose poor nutritional status not only had failed to improve after the operation but had continued to deteriorate.

CLINICAL SYMPTOMATOLOGY

The clinical symptomatology includes postprandial fullness and nausea, eructation and belching, weakness, fatigue, dizziness, constipation or diarrhea, and chiefly inability to gain weight and to work. In order of frequency these symptoms were encountered as follows (see Table II): Weakness and/or marked fatigue, especially in association with meals, was encountered in fourt-

TABLE II. OCCURRENCE OF SYMPTOMS

NO.	NAME	WEAKNESS FATIGUE	POST-PRANDIAL FULLNESS AND/OR NAUSEA	ERUCTATION AND BELCHING	DIZZINESS	CONSTIPATION	DIARRHEA	VITAMIN DEFICIENCY
1	C. M.	+	+	+	+	+	–	–
2	G. S.	+	+	+	+	+	–	–
3	L. Z.	+	+	+	+	+	–	–
4	J. K.	+	+	+	+	+	–	+
5	M. C.	+	+	+	+	–	–	+
6	S. R.	+	+	–	–	–	–	–
7	S. Z.	+	+	+	+	–	–	–
8	B. E.	+	+	+	+	+	–	–
9	B. B.	+	+	+	+	+	–	+
10	L. R.	+	+	+	–	+	+	–
11	F. M.	+	–	+	+	–	–	–
12	R. B.	+	–	–	–	–	+	+
13	A. F.	+	+	+	+	+	–	–
14	O. S.	+	+	+	+	–	–	–

teen patients and represented one of the most frequent complaints. Postprandial fullness and/or nausea was present in twelve patients. Eructation and belching was a complaint of twelve patients. Dizziness at various times of the day but mostly in connection with the intake of food was found in eleven patients. In association with dizziness, profuse perspiration, palpitations, and increasing weakness occurred often forcing the patient to lie down after meals in order to avoid fainting. Tendency to constipation was found in eight patients, to diarrhea in two patients.

Marked signs of vitamin deficiency were present in four individuals who presented sore mouth with reddening and hypertrophy of the papillae of the tongue and in one case cheilosis. The other individuals showed only minor signs of nicotinic acid and riboflavin deficiency of the mucous membrane of the mouth as well as mild evidence of vitamin A deficiency (dry skin with hyperkeratosis and folliculitis).

It has to be mentioned that in a few of our patients additional clinical findings were present. One patient (Case 7) showed restricted motility of the left diaphragm due to a lung injury suffered during World War I. Another (Case 8) had bronchiectasis with shrinkage of the right lower lobe. One patient (Case 12) presented evidence of mild arthritis with hyperuricemia and was suspected of having gout. One patient (Case 13) had a history of malaria and evidence of mild thromboangiitis obliterans. Case 14 was mentioned as a case of gastric syphilis; the patient's Wassermann reaction remained positive after intensive treatment. It is important to emphasize that the majority of these individuals presented stigmas of psychoneurosis with tendency to overemphasis and fixation of symptoms. Although some of them were inclined to attribute their "nervousness" to the poor general condition and loss of weight, psychoneurotic trends could be traced back to the period preceding the operation and the onset of the disease.

BLOOD MORPHOLOGY AND BLOOD PROTEINS

Morphologic blood studies failed to reveal any striking abnormality. The red blood count ranged from 3,790,000 to 5,620,000, the average being 4,436,000.

TABLE III. BLOOD MORPHOLOGY AND BLOOD PROTEINS

NO.	NAME	HEMOGLOBIN (%)	ERYTHROCYTES (IN MILLIONS)	TOTAL PROTEIN OF SERUM (IN GM. %)	ALBUMIN (IN SERUM GM. %)	GLOBULIN (IN SERUM GM. %)
1	C. M.	85	4.65	6.3	5.0	1.3
2	G. S.	80	4.10	5.6	4.4	1.2
3	L. Z.	70	4.15			
4	J. K.	78	4.25	4.6	3.1	1.5
5	M. C.	85	4.51	6.1	4.4	1.7
6	S. R.	79	4.42			
7	S. Z.	85	4.62	6.1	4.7	1.4
8	B. E.	77	4.12			
9	B. B.	85	4.48	5.5	4.5	1.0
10	L. R.	92	4.71	5.3	3.5	1.8
11	F. M.	101	5.62	7.4		
12	R. B.	70	3.79	6.8	4.3	2.5
13	A. F.	93	4.51			
14	O. S.	78	4.18			

The hemoglobin figures ranged from 70 to 101 per cent, the average being 83 per cent (see Table III). In some of the cases there was a tendency to a moderate anemia of the hypochromic type (Cases 3 and 12). There were no abnormalities in the white blood count. The serum protein figures ranged from 4.6 to 7.4 Gm. per cent, the average being 6 Gm. per cent, which is a low normal figure for the hospital population. Only one patient (Case 4) had a low concentration of serum proteins (4.6 Gm. per cent). The albumin concentration ranged from 3.1 to 5 Gm. per cent (average 4.2 Gm. per cent), the globulin concentration from 2 to 2.5 Gm. per cent (average 1.6 Gm. per cent). Thus, the average albumin-globulin ratio appeared to be within normal limits.

GASTRIC ACIDITY

Gastric acidity studies were performed in each case with one exception. This patient (Case 14), in whom a total gastrectomy with esophagojejunostomy for gastric syphilis had been performed, was not studied. The test meals consisted in eleven cases of 150 c.c. of a 5 per cent alcohol solution, in one case of gruel, and in one case of bouillon. The gastric juice was collected at fifteen-minute intervals for two hours. Of the thirteen examined patients eight failed to reveal the presence of any free hydrochloric acid, while in the remaining five the figures of free hydrochloric acid varied from 14 to 32 units. The total acidity ranged from 9 to 42 units (see Table IV). There was no correlation between the lack of gastric acidity and the occurrence of gastric symptoms or hypochromic anemia. While one patient (Case 3) presented normal figures of gastric acidity, another (Case 12) had no free hydrochloric acid.

ROENTGEN STUDIES

Roentgen studies of the gastrointestinal tract were performed in all cases and particular attention was paid to the function of the stoma, the motility of the gastric stump, and of the small intestine. The stoma was patent in all cases and the majority presented rapid evacuation of the gastric stump. Only one patient (Case 10) developed a marginal ulcer in the later course, for which he

TABLE IV. GASTRIC ACIDITY

NO.	NAME	GASTRIC ACIDITY HIGHEST FIGURES	
		FREE ACIDITY	TOTAL ACIDITY
1	C. M.	0	14
2	G. S.	30	42
3	L. Z.	26	42
4	J. K.	0	9
5	M. C.	0	12
6	S. R.	14	26
7	S. Z.	0	14
8	B. E.	0	24
9	B. B.	0	12
10	L. R.	32	46
11	F. M.	0	15
12	R. B.	0	14
13	A. F.	16	24
14	O. S.	-	-

had to be rehospitalized. In none of the other cases was there evidence of a gastrojejunal ulcer. Special small intestine studies were performed in seven cases and failed to reveal abnormalities. A distention of the upper jejunal loops could be observed in most of the cases. There was, however, no evidence of a disturbed small intestine motility or a deficiency pattern.

In a few individuals the stools were carefully analyzed for presence of undigested food elements. Only rarely larger amounts of fatty acids and soaps, in absence of neutral fat, and occasionally undigested muscle fibers were found, while undigested starch cells did not exceed the normal limits. None of the examined patients presented frothy, bulky stools indicative of steatorrhea.

FASTING BLOOD SUGAR LEVELS AND GLUCOSE TOLERANCE TESTS

The fasting blood sugar was determined in all fourteen cases and was followed in thirteen patients by a glucose tolerance test with oral administration of 100 Gm. of glucose. In one of the patients (Case 12) it was impossible to perform the glucose tolerance test because the administration of glucose caused, on repeated occasions, violent vomiting. It must be stated that the majority of the other patients complained of nausea and epigastric discomfort shortly after the intake of glucose and in a few instances vomiting could be prevented only by placing the patient in a horizontal position. The fasting blood sugar ranged between 70 to 146 mg. per cent, the average being 101 mg. per cent (see Table V). Two of the patients had a moderate elevation of the fasting blood sugar (Cases 6 and 9), in only three instances was the fasting blood sugar below 80 mg. per cent, and in no instance was it lower than 70 mg. per cent. The curves obtained in the sugar tolerance test were characterized by an early peak which was reached usually after one-half hour and in only three instances one and one-half hour after glucose intake. The maximum elevation ranged from 130 to 258 mg. per cent, the average being 188 mg. per cent. In all instances there was a rapid drop of the blood sugar after two and one-half to three and one-half hours to comparatively low figures, ranging from 51 to 80 mg. per cent, the average being 60 mg. per cent. The glucose tolerance test in the gastrectomized patients was thus characterized by a steep and rapid elevation of the blood sugar level with

TABLE V. GLUCOSE TOLERANCE TESTS

NO.	NAME	BLOOD SUGAR IN MG. PER CENT				
		FASTING	30 MIN.	90 MIN.	150 MIN.	210 MIN.
1	C. M.	89	180	113 (5.0%)	78	55
2	G. S.	79	168	145 (0.9%)	105	57
3	L. Z.	74	164	71	66	58
4	J. K.	105	200 (2.2%)	170 (3.5%)	75 (0.1%)	51
5	M. C.	88	160	200 (5.0%)	90 (3.5%)	59
6	S. R.	130	200 (tr.)	160 (1.2%)	79 (tr.)	58
7	S. Z.	119	150	115	72	51
8	B. E.	110	188 (3.3%)	220 (7.5%)	150 (6.0%)	59 (0.8%)
9	B. B.	146	197	258 (2.3%)	78 (0.7%)	60
10	L. R.	118	198 (3.5%)	160 (5.0%)	89 (0.5%)	80
11	F. M.	89	130	110	86	59
12	R. B.	70	–	–	–	–
13	A. F.	91	180	120	89	60
14	O. S.	99	200	170	101	70

The figures in parentheses indicate sugar concentration in the urine in Gm. per cent. The other urine specimens were sugar-free.

a subsequent steep drop to levels ranging around 60 mg. per cent. Glycosuria was absent in all individuals prior to the glucose tolerance test. In eight of the thirteen patients considerable amounts of sugar were spilled in the course of the test, ranging from 0.9 to 7.5 Gm. per cent, the average being 3.6 Gm. per cent. A glycosuria to this extent is certainly striking in nondiabetic individuals.

Most of the patients experienced gastric and general symptoms after the administration of glucose, which resembled their usual postprandial complaints. These symptoms occurred in the first hour of the test, subsided usually in the second to recur, frequently in even severer but somewhat different form, in the third to fourth hour. The early symptoms were described as pressure, fullness, and nausea and led occasionally to vomiting; the late symptoms consisted chiefly of palpitations, headaches, dizziness, and perspiration and thus resembled closely the classical sympatomatology of hypoglycemia.

VITAMIN A SERUM LEVELS AND VITAMIN A TOLERANCE TEST

The vitamin A concentration of the fasting serum was determined in twelve patients. The figures ranged from 42 to 108 μg per cent, the average being 66 μg per cent (see Table VI). This is a normal level and compares well with the

TABLE VI. VITAMIN A TOLERANCE TESTS

NO.	NAME	VITAMIN A IN SERUM IN μG PER CENT	
		FASTING	4 HR. AFTER 180,000 I.U. OF VITAMIN A
1	C. M.	48	85
2	G. S.	80	172
3	L. Z.	42	195
4	J. K.	90	122
5	M. C.	60	151
6	S. R.	86	107
7	S. Z.	45	120
8	B. E.	48	102
9	B. B.	58	160
10	L. R.	–	–
11	F. M.	56	63
12	R. B.	72	188
13	A. F.	108	168
14	O. S.	–	–

average fasting vitamin A level of the hospital population (60 to 80 μg per cent). The vitamin A tolerance test with 180,000 I.U. of vitamin A followed the determination of the fasting level. The vitamin A serum concentration after four hours ranged from 63 to 195 μg per cent, the average being 136 μg per cent. Thus, the response to the vitamin A tolerance test has to be considered normal for the average patient. The character of the curve presents a normal elevation with one exception, the flat curve in Case 11.

COMMENT

Gastroenterologists as well as surgeons have recently become interested in the symptomatology of some gastrectomized individuals whose symptoms are not caused by a marginal ulcer and who, according to various statistics, represent 6 to 29 per cent of all patients subjected to partial gastrectomy for peptic ulcer.

A group of such patients, referred to the Nutrition Clinic of the Mount Sinai Hospital chiefly because of inability to gain weight, were subjected to a careful study. The average patient of this group had lost 15.9 pounds from the onset of ulcer symptoms to the time of the operation and, in addition, 10.1 pounds after the gastrectomy, the total loss of weight being 26 pounds. These individuals had been placed on various types of high caloric diets, supplemented by vitamin concentrates and liver extract, but failed to gain weight. Each of them presented a definite nutritional problem.

The postgastrectomy syndrome was characterized by postprandial fullness, nausea and dizziness, eructation and belching, fatigue, weakness, palpitations, perspiration, headaches, and tendency to fainting spells. A thorough analysis of these symptoms permitted a classification into early and late postprandial symptoms. The early symptoms were chiefly fullness, nausea, eructations, belching, dizziness, and tendency to vomiting, while the late symptoms occurring usually two to four hours after meals were dizziness, palpitations, perspiration, headaches, fatigue, and weakness. The early as well as the late symptoms were somewhat relieved by the assumption of a horizontal position. Because of these complaints many of the patients developed the habit of resting for various periods of time after meals. It is of interest that in many patients the late symptoms could be definitely relieved by eating while the early symptoms precluded any further food intake. The appearance of early symptoms compelled these individuals to restrict their food intake to very small amounts; the relief of late symptoms by eating taught them to take these small amounts of food at frequent intervals. One gained the impression that the early and the late postprandial symptoms were caused by different mechanisms.

Clinical observation of these individuals and a study of their case histories revealed evidence of psychoneurotic stigmas in all of them. Many of them were already stomach conscious before the operation and the shock of the operation, the immediate postoperative course with its occasional complications, the general rundown condition and malnutrition, and especially the postprandial symptoms described previously exaggerated the pre-existing stomach awareness and led gradually to a vicious circle wherein the postprandial symptoms and the fear to eat were the outstanding factors. In the extremely severe cases

the final picture may then, physically as well as psychologically, resemble that of anorexia nervosa: the patient appears underweight, there is diminished turgor of the skin, the eyes are deeply set; he is morose, self-centered, and full of anxiety and hypochondriac ideas centering about the stomach. The basal metabolic rate may be low, as exemplified by the patient (Case 4) whose basal metabolic rate ranged between –11 to –19 per cent.

The morphologic blood picture was practically normal with an occasional tendency to hypochromic microcytic anemia. Berkman and Heck[5] and others have found this type of anemia more frequently among their gastrectomized patients, while Farris, Ransom, and Coller[8] encountered it, as we did, only occasionally. The blood proteins as well as the partition were normal with one exception. There were only mild signs of nutritional deficiency consisting of smoothness and reddening of the tongue. In the latter cases there was moderate hypertrophy of the papillae, occasional cheilosis, moderate hyperkeratosis, and folliculitis of the skin.

Roentgen studies of the gastrointestinal tract failed to reveal any abnormality in the function of the stoma or of the small intestine. The majority showed rapid evacuation of the gastric stump with the usual subsequent overfilling of upper jejunal loops. One patient developed a marginal ulcer in the later course.

The fasting blood sugar averaged 101 mg. per cent. Only in three cases was the fasting blood sugar below 80 mg. per cent and in no instances lower than 70 mg. per cent. There was no evidence of hypoglycemia or hypoglycemic symptoms in the fasting state. The glucose tolerance curve showed usually rapid and steep elevation up to 258 mg. per cent, with an average level of 188 mg. per cent, and a rapid steep drop to an average of 60 mg. per cent two and one-half to three and one-half hours after the glucose test meal. In the course of the test a considerable number of individuals eliminated glucose in the urine in concentrations ranging from 0.9 to 7.5 Gm. per cent. Since none of these patients had diabetes, the extent of the glycosuria was remarkable and had to be attributed to the rapid absorption of sugar from the intestinal wall and the transient elevation of the blood sugar level over the normal kidney threshold for glucose. The possibility, however, of a pancreatic origin of some of the high blood sugar curves in connection with a pre-existing penetrating duodenal ulcer and a probable injury to the pancreas cannot be excluded.

The question arises whether any relationship exists between the pattern of the glucose tolerance test and the patient's symptoms. Glaessner[9] attributed the early postprandial symptoms to a hyperglycemic shock. We are inclined to doubt the importance of hyperglycemia in this connection since there is no other instance known in which hyperglycemia would lead to similar symptoms of shock. We would rather attribute the early phase of postprandial symptoms to mechanical factors: the small stomach, the rapid emptying of the stump, the rapid filling and distention of the jejunum, and the subsequent mesenteric irritation. The late postprandial symptoms, however, are in all probability closely related to chemical factors and to the rapid and steep decrease of the blood sugar level. In their clinical manifestations the late symptoms resemble the typical state of hypoglycemia and are relieved by food intake. Interestingly enough, the symptoms of these patients can be reproduced experimentally by the glucose

tolerance test: in the early stage of the test epigastric pressure, fullness, nausea, and occasional vomiting are encountered; in the late stage of the test, palpitations, headaches, dizziness, and perspiration occur. One has to consider, however, that symptoms of hypoglycemia are not infrequently encountered in ulcer patients not operated upon and occasionally in apparently normal individuals. Evensen[10] found hypoglycemic symptoms in 30 per cent of his patients with gastroenterostomy, in about 15 per cent of patients with resected stomachs, in 8 per cent of patients suffering from peptic ulcer not operated upon, and in 6 per cent of normal individuals. Glucose deficiency has been considered to be the cause of fatigue and weakness by many authors (Wilder,[11] Gillespie,[12] Portis and Zitman,[13] Alexander and Portis,[14] and Karlan and Cohn[15]).

In the light of these findings the mechanism of the postprandial symptoms may be explained as follows: after the intake of food there occurs rapid filling and distention of the small stomach, rapid emptying of the stomach stump, and overflooding of the jejunum, causing rapid absorption of carbohydrates and steep elevation of the blood sugar level. In this stage the symptoms are probably due to mechanical factors (and in some cases possibly to the absorption of unchanged proteins with the subsequent effect of shock). The posthyperglycemic hypoglycemia is probably the chemical cause of the late symptoms. This tendency to hypoglycemia in these patients is probably caused by a multiplicity of factors. The rapid and early elevation of the blood sugar level per se (caused by the rapid emptying of the stomach) is probably one of them, since it is known that there exists a reciprocal relationship between the height of the hyperglycemic rise and the depth of the later hypoglycemic phase. The tendency of ulcer patients who were not operated upon to hypoglycemia may be another factor. Whether or not the ulcer patient develops this occasional disturbance of carbohydrate regulation on the basis of some central neurogenic or psychogenic factors cannot be discussed here. While Alexander and Portis[14] are of the opinion that emotional factors are responsible for hypoglycemia via the vagus nerve, Karlan and Cohn[15] found that the state could not be blocked by atropine.

There is another factor that must be taken into consideration. It is known that the preceding diet affects the character of the glucose tolerance test: high carbohydrate, low fat diet flattens, while low carbohydrate high fat diet raises the glucose tolerance curve. Ulcer diets are, as a rule, high fat diets and their use prior to the test may be another factor responsible for the blood sugar pattern.

The examination of the vitamin A serum concentration and vitamin A tolerance tests revealed, as a rule, normal figures; in only one instance a flat curve was encountered, resembling the vitamin A tolerance curves found in sprue.[16] Occasionally, larger amounts of unabsorbed fatty acids and soaps and moderate amounts of undigested muscle fibers were found in the stools, while evidence of a disturbed starch absorption was not present. In not a single case, however, did the stools resemble the frothy, bulky, light-colored stools of sprue.

Flat glucose tolerance curves are occasionally found following gastric resection. We observed it in three gastrectomized patients who could not be included in this study. These findings may indicate that in some individuals dis-

turbed intestinal absorption is a factor, which should not be overlooked and which certainly deserves further study (see Wollaeger, Comfort, Weir, and Osterberg[17]).

SUMMARY

1. A group of fourteen patients, who for many years after partial gastrectomy for ulcer had been unable to gain weight and presented difficult nutritional problems, have been investigated. The symptoms were analyzed and divided in two groups: early and late postprandial symptoms.

2. The early symptoms were caused by mechanical factors, small stomach and rapid emptying, and overflooding of the small intestine. The late symptoms were due to chemical factors, hypoglycemia secondary to the exaggerated postprandial hyperglycemia, and occasionally secondary to disturbed intestinal absorption.

3. The postgastrectomy syndrome was caused by a sequence of these early mechanical and late chemical factors, exaggerated by distinct psychoneurotic stigmas. Many of these individuals were stomach conscious. The shock of the operation, the postoperative course, later the postgastrectomy symptoms, and finally the diminished physical and mental resistance associated with underweight and malnutrition exaggerated the stomach awareness. The ultimate effect was a conflict between the postprandial symptoms, the late manifestations of which are relieved by food, and the fear to eat. The treatment of these patients presents a series of difficult clinical, nutritional and psychologic problems, all of which require consideration.

REFERENCES

1. Jordan, S. M.: End Results of Radical Surgery of the Gastrointestinal Tract as Seen by Gastroenterologist, J. A. M. A. **116**: 586, 1941.
2. Mateer, J. G.: Discussion on Jordan.[1]
3. Miller, G. G.: Report on 230 Cases of Subtotal Gastric Resection for Gastric Ulcer, SURGERY **12**: 383, 1942.
4. Custer, M. D., Butt, H. R., and Waugh, J. M.: The So-Called Dumping Syndrome After Subtotal Gastrectomy: A Clinical Study (Unpublished Data), quoted by Berkman and Heck.[5]
5. Berkman, J. M., and Heck, F. J.: Symptoms Following Partial Gastric Resection, Gastroenterology **5**: 85, 1945.
6. Sandweiss, D. J., Sugarman, M. H., Podolsky, H. M., and Friedman, M. H. F.: Nocturnal Gastric Secretion in Duodenal Ulcer, J. A. M. A. **130**: 258, 1946.
7. Crohn, B. B.: Discussion on Sandweiss et al.[6]
8. Farris, J. M., Ransom, H. K., and Coller, F. A.: Total Gastrectomy: Effects Upon Nutrition and Hematopoiesis, SURGERY **13**: 823, 1943.
9. Glaessner, C. L.: Hyperglycemic Shock, Rev. Gastroenterol. **7**: 528, 1940.
10. Evensen, O. K.: Alimentary Hypoglycemia After Stomach Operations and Influence of Gastric Emptying on Glucose Tolerance Curve, Acta med. Scandinav., 1942 (suppl. 126), quoted in Lancet **2**: 626, 1942.
11. Wilder, J.: Psychological Problems in Hypoglycemia, Am. J. Digest. Dis. **10**: 428, 1943.
12. Gillespie, R. D.: An Investigation Into the Symptoms and Signs of Fatigue and Exhaustion, Guy's Hosp. Rep. **79**: 92, 1929.
13. Portis, S. A., and Zitman, I. H.: A Mechanism of Fatigue in Neuropsychiatric Patients, J. A. M. A. **121**: 569, 1943.
14. Alexander, F., and Portis, S. A.: A Psychosomatic Study of Hypoglycemic Fatigue, Psychosom. Med. **6**: 191, 1944.
15. Karlan, S. C., and Cohn, C.: Hypoglycemic Fatigue, J. A. M. A. **130**: 553, 1946.
16. Adlersberg, D., and Sobotka, H.: Fat and Vitamin A Absorption in Sprue and Jejunoileitis, Gastroenterology **1**: 357, 1943.
17. Wollaeger, E. E., Comfort, M. W., Weir, J. F., and Osterberg, A. E.: The Total Solids, Fat and Nitrogen in the Feces: II. A Study of Persons Who Had Undergone Partial Gastrectomy With Anastomosis of the Entire Cut End of the Stomach and the Jejunum (Polya Anastomosis), Gastroenterology **6**: 93, 1946.

THREE HUNDRED SEVENTY-FOUR ACUTE WAR WOUNDS OF THE THORAX

CHARLES B. BURBANK, M.D.,* BOSTON, MASS., WILLIAM H. FALOR, M.D.,* AKRON, OHIO, AND HOWARD W. JONES, JR., M.D.,* BALTIMORE, MD.

THIS paper presents the experience of a number of teams of the Fifth Auxiliary Surgical Group in the treatment of 374 intrathoracic wounds in the European Theatre of Operations from Sept. 16, 1944, to May 15, 1945. Combined wounds of the thorax and abdomen are not included, as they are reported elsewhere.[1]

Two hundred and eighty-three individuals were treated in Field Hospitals with an average time between injury and operation of about seven hours. The remaining ninety-one were taken to Evacuation Hospitals with an average time between injury and operation of ten hours.

Preoperative Care.—Patients were admitted directly to the hospital shock ward and there prepared for operation. The treatment of individuals with penetrating or perforating wounds of the thorax was complicated not only by severe shock but by certain special problems associated with thoracic injuries. The treatment of shock differed little from that employed for wounds elsewhere in the body and will not be recounted. Reference may be made to other papers for details.[2] The special problems involved in the preoperative treatment of casualities with thoracic wounds will be considered at length.

The incidence of injury according to the standard method of wound classification is given in Table I.

The principal emphasis in the treatment of sucking wounds has been placed on immediate closure as a lifesaving measure. For present statistical purposes every wound has been considered as a sucking wound if (1) it was reported as sucking on the Emergency Medical Tag previous to reception in the hospital, whether or not it was sucking when the dressing was removed, and if (2) it was sucking spontaneously in the hospital.

Although no one can deny the urgency of closing a sucking wound, once it is sealed by petrolatum gauze no priority for definitive care need be given. This is borne out by reference to Table II in which the same mortality for both the sucking and nonsucking groups of cases is shown.

Hemothorax occurred in 79 per cent of the cases. In the 289 cases in which it was present there were up to 2,500 c.c. of blood. The preoperative treatment was and should be conservative. A small collection of blood, 200 to 300 c.c., in the absence of other factors, was left alone. If respiratory embarrassment dictated aspiration before definitive care could be instituted, aspiration with a large needle was done. If hemothorax rapidly recurred, high priority was given for an immediate operative procedure. At the time of

Received for publication, June 21, 1946.

*Formerly Major, Medical Corps, Army of the United States.

TABLE I. WOUND STATISTICS—374 PATIENTS

Causative agent		
Gunshot wounds		193
Shell fragment wounds		181
Location		
Left		180
Right		189
Bilateral		5
Type		
Penetrating		213
Sucking	120	
Nonsucking	93	
Perforating		161
Sucking	61	
Nonsucking	100	

aspiration no air was reinjected into the pleural cavity. An intrapleural injection of 40,000 units of penicillin routinely followed aspiration.

In some instances where a thoracotomy was not indicated and the wound did not require débridement as with perforating gunshot wounds, aspiration of the hemothorax constituted the principal method of therapy.

Pneumothorax per se was not treated in the preoperative ward unless respiratory embarrassment was present. Under this circumstance there was no hesitancy in doing a simple aspiration.

TABLE II. COMPARISON OF SUCKING AND NONSUCKING WOUNDS

SUCKING			NONSUCKING		
NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
181	15	8.3	193	16	8.3

Tension pneumothorax was an unusual preoperative complication occurring but thirty-two times. In the majority of cases it was due to a valvelike type of sucking wound and in the remainder to a punctured lung. Although the former type of injury could be treated by sealing the wound and aspiration, the uncertainties of diagnosis required the introduction of a large needle or a stiff catheter into the second intercostal space anteriorly. This was attached to a drainage apparatus with water seal.

Anesthesia.—In thoracic casualties anesthesia was of great importance. In the presence of a sucking wound or an intrathoracic procedure, endotracheal gas, oxygen, and ether was the anesthetic of choice. A preliminary induction with penthothal sodium was frequently used. This obviated a period of excitement which might reopen a temporarily sealed sucking wound or start fresh bleeding from the lung. Either of these complications made the further administration of anesthesia very difficult and hazardous.

The advantage of being able to use positive pressure for expanding the lung and to stabilize the mediastinum during intrathoracic surgery is so great that further justification of endotracheal anesthesia is unnecessary. The various kinds of anesthetics used are shown in Table III. Among the 281 endotracheal anesthesias there were twenty-six deaths, a mortality of 9 per cent. None of these were considered directly attributable to the anesthetic.

TABLE III. TYPE OF ANESTHETIC EMPLOYED

ANESTHETIC	IN ALL WOUNDS		IN SUCKING WOUNDS	
	NUMBER OF CASES	PER CENT	NUMBER OF CASES	PER CENT
Endotracheal gas-oxygen-ether	261	75	140	78
Local	83	22	27	14
Pentothal sodium	6	2	5	3
Gas-oxygen	4	1	9	5

Operative Management of Thoracic Wounds.—The criteria for the operative treatment of intrathoracic wounds changed during the campaign in Western Europe. In the beginning, the general tendency was towards the radical view and consequently there were few patients who did not undergo thoracotomy. It was found, however, at busy times when abdominal and thoracoabdominal wounds were considered to have a high priority, that some chest wounds could be cared for by less radical procedures. This led to the formation of the following definite indications for thoracotomy.

1. Hemothorax due to active bleeding. These patients were usually in severe shock on admission and did not respond well to shock therapy. The source of bleeding was either an intercostal or internal mammary vessel, the lung, or more rarely the heart or mediastinal structures (Table IV).

TABLE IV. ACTIVE INTRATHORACIC HEMORRHAGE DEMONSTRATED AT OPERATION IN FIFTY CASES

	NUMBER OF CASES	PER CENT
Source		
Lung	33*	66
Intercostal vessel	16	32
Internal mammary vessel	2	4
Causative agent		
Shell fragment	32	64
Gunshot	18	36

*One case combined hemorrhage both from lung and intercostal vessel.

2. Hemothorax which could not be aspirated, usually due to clotted blood. These patients often showed dyspnea, cyanosis, and mediastinal shift. Under these circumstances an open thoracotomy was undertaken to prevent organization of the blood and the possible necessity for a decortication of the lung at a later date.

3. The presence of a foreign body 2 cm. or larger in the lung parenchyma or pleural cavity. Such particles were removed to obviate the danger of lung abscess or infected hemothorax.

4. The presence of shattered rib fragments either in the lung or pleural cavity or large fragments which had not perforated the pleura. These indicated thoracotomy or extrapleural rib resection. It should be added that many surgeons came to feel that bone fragments in the lung were of more serious consequence than metallic foreign bodies.

5. Tension pneumothorax due to a bronchopleural fistula required thoracotomy for lung suture.

A sucking wound was not considered an indication for a thoracotomy. Débridement and closure were performed unless one of the previously mentioned indications for thoracotomy was present also. With these indications for thoracotomy, treatment was in general more conservative. However, it was observed that the more radically treated patients often had smoother postoperative courses. Temperature and pulse elevations were less as a result of the operative removal of all serum and blood, both liquid and clotted. Postoperation serum collections were readily aspirated so that a high percentage of individuals could be evacuated with a dry pleural cavity and completely re-expanded lung. Furthermore, reports from general hospitals indicated that in those patients treated conservatively the incidence of empyema, lung abscess, and infected hemothorax was greater than in those treated radically. This was especially true in the presence of small foreign bodies. Finally, directives from the surgeons office stated that all foreign bodies of whatever size should be removed because of the high incidence of late lung abscess and empyema.

Thus, toward the end of the War in Europe foreign bodies of a size large enough to find and suspected lung lacerations especially from shell fragment wounds were added to the indications for thoracotomy. In spite of the wider indications for thoracotomy, the majority of cases did not require this procedure.

In sixty-five instances, comprising mainly perforating gunshot wounds, a dry dressing was the only treatment necessary for the wound.

In 167 cases a débridement was the only procedure carried out. This included both sucking and nonsucking wounds and many times resulted in the conversion of a nonsucking wound to a sucking one. It was therefore often an arbitrary decision as to whether a given case should be classified as an extensive débridement or a thoracotomy through the wound.

In thirty-two instances a trocar thoracotomy with the establishment of tube drainage was added to one of the previously mentioned procedures, and it is our opinion that this procedure might have been used more often.

In 142 incidences, or 38 per cent of the cases, a formal thoracotomy was done. Operative procedures varied according to the pathology. Lacerations of the lung were sutured, foreign bodies removed, rib fragments excised, blood and clot evacuated. One pneumonectomy was performed for severe laceration of both the upper and lower lobes; convalescence was uneventful. In another instance a large laceration was sutured, and on re-expansion of the lung with positive pressure there was a massive intrabronchial hemorrhage resulting in death of the patient. In retrospect a lobectomy should have been performed on this patient. The indications for such radical surgery, however, were rare.

The location of the incision was seldom troublesome; in most instances it was made at the wound of entrance. If there was extensive rib damage entrance was made through the bed of a resected rib; if little or no rib damage was present an intercostal incision was made. When there was reason to have access to a part of the chest not readily available through an enlargement of the wound, no hesitancy was felt in doing a simple débridement and closure followed by a thoracotomy through an incision that would give access to the

desired area. For example, there was a case in which a bullet entered the upper right chest and finally lodged in the lower lobe of the right lung; the wound of entrance was closed and a formal intercostal thoracotomy performed at the optimum level both for the removal of the foreign body and the examination of the entire right lung.

A sucking wound at the apex of the lung anteriorly commanded special attention as it could easily be mistaken for a perforation of the trachea. Approach to this area was difficult but could be accomplished by a division of the clavicle and elevation of the fragments.

A perforating wound of the wing of the scapula was also troublesome as it was frequently difficult to evaluate the extent of injury to the chest wall. The most satisfactory operation could be done by elevating the scapula through a thoracoplasty incision. Many times a wound which was not sucking exteriorly was found to do so as the scapula was elevated.

Thoracotomy incisions were closed with pericostal silk or wire sutures and the soft tissues with catgut. Following débridement small wounds were closed in layers with catgut.

Regardless of the procedure required by the wound itself, the aspiration of blood from the pleural cavity was considered a necessary part of the definitive care. Many times this was done with an aspirating needle. It was not considered necessary to remove the entire amount at one sitting and frequent postoperative aspirations were the rule.

The question of tube drainage was perplexing and debated. Difference of opinion arose not so much concerning the desirability of the procedure which was conceded but because of the lack of constant and meticulous postoperative care so necessary to the satisfactory operation of the water-seal drainage. For this reason the number of drainage tubes was less than would be required under more ideal circumstances. If tube drainage was used a No. 28 or 30 rubber catheter or tube was employed. The tip with numerous holes was sutured high on the anterior parietal wall. Sometimes constant suction was attached to help remove the fluid and re-expand the lung.

Following major procedures bronchoscopic aspiration was frequently used on the operating table.

In the 142 major procedures (almost all thoracotomies) there were twelve deaths, a mortality of 8.4 per cent. In the remaining 232 cases there were nineteen deaths, a mortality of 8.2 per cent.

Heart Injuries.—There were four individuals with injuries to the heart muscle.

CASE 1.—There was a small laceration of the left ventricle. The wound of entry was sucking through the left fifth interspace. Through an anterior approach the laceration was sutured with fine silk and the pericardium loosely closed. Recovery was uneventful.

CASE 2.—There was a sucking wound of entrance through the right fourth rib. A shell fragment had passed through the lower lobe and out posteriorly. There was a laceration of the right atrium and of the right phrenic nerve. The perforating wound of the lower lobe of the right lung was repaired and the heart laceration was sutured with fine silk. The pericardium was loosely closed and the chest was drained. Recovery was uneventful.

CASE 3.—There was a penetrating sucking wound in the left seventh interspace in the anterior axillary line. In addition there were multiple penetrating wounds of the back and thighs. A débridement and closure of the chest wound was done. The patient died suddenly on the operating table. Autopsy revealed a shell fragment lodged in the wall of the left ventricle having lacerated the ramus descendens of the left coronary artery. A foreign body had been noted in the anteroposterior chest plate but was thought to be in the mediastinum.

CASE 4.—There was a penetrating chest wound similar to that in Case 3. The wound of entrance was in the right upper chest. By x-ray there was a foreign body lying in the center of the heart shadow, and in the lateral view it was thought to be in the posterior mediastinum. At thoracotomy a laceration of the right upper lobe was found but the patient died suddenly on the operating table. Autopsy revealed a shell fragment 25 by 15 by 10 mm. in the right ventricle. The foreign body had entered the superior vena cava, passed through the auricle, and perforated the tricuspid valve as it entered the ventricle.

Bilateral Thoracic Wounds.—There were five patients with bilateral intrathoracic injury, two of whom died.

CASE 1.—There were bilateral perforating wounds of the chest and both wounds of exit were sucking. The patient was critically ill. All wounds were débrided and closed under local anesthesia. After doing well for seven days the patient suddenly died. An autopsy revealed a secondary hemorrhage from a lacerated azygous vein.

CASE 2.—This patient was wounded by one bullet which entered the right chest anteriorly and left through the left chest posteriorly. Neither wound was sucking, and débridement and closure were done under local anesthesia. Recovery was uneventful.

CASE 3.—In this case the bullet passed through both chests from right to left superiorly. Bilateral thoracotomies were performed. This is the only case of such a combined operation recorded in the series. The left upper lobe only was injured. The postoperative course was satisfactory.

CASE 4.—In this case a bullet entered through the right chest and penetrated into the left. The wound of entry was sucking and was débrided and closed. A thoracotomy was performed on the left side and the foreign body removed. Recovery was uneventful.

CASE 5.—There was a perforating wound caused by a missile proceeding from right to left. The sternum was fractured and depressed, and there were bilateral sucking wounds. The sternum was elevated with constant traction, and the wounds were closed. The patient developed bilateral pneumothorax which could not be controlled by continuous aspiration and died of anoxia on the third day.

In addition to the myocardial injuries there were three lacerations of the pericardium without myocardial damage. These lesions were sutured without mishap. One patient died from a complicating skull injury.

Esophageal Wounds.—There were three patients with wounds of the thoracic esophagus. Each wound was sutured with catgut. All recovered.

Postoperative Care.—Thoracic wounds require certain special postoperative procedures in addition to intravenous blood and plasma to combat shock, morphine for pain, penicillin, and sulfadiazine. Many patients had tube drainage and constant care was required to keep the water-seal drainage system in operating order. From time to time cases were discovered with drainage tubes open to the air. Fortunately no death was attributed to this cause.

In cases without the tube drainage, and in some with, it was routine to aspirate with needle and syringe any accumulation of intrathoracic fluid. This was done daily or more often if necessary. It was routine to inject 40,000 units of penicillin into the pleural cavity after each aspiration. It was attempted to evacuate patients from the fifth to tenth postoperative day with a dry thoracic cavity.

Unless pressing circumstances prevailed all thoracic wounds had bronchoscopic aspiration before leaving the operation table. Bronchial obstruction was often troublesome and daily or more frequent aspiration was lifesaving in some cases.

A Levine tube with suction was routine for forty-eight hours to prevent gastric dilatation.

Oxygen via B.L.B. masks was used when necessary.

Mortality.—In the 374 cases there were thirty-one deaths, a mortality rate of 8.2 per cent.

The types of wounds encountered in the fatal cases are shown in Table V. There were ten major thoracotomies, nineteen débridements and simple closures, one anterior mediastinotomy, and the elevation of one compound fracture of the sternum.

TABLE V. WOUND STATISTICS IN THIRTY-ONE FATAL CASES

Causative agent		
Gunshot wounds		6
Shell fragment wounds		25
Location		
Left		15
Right		14
Bilateral		2
Type		
Penetrating		16
Sucking	10	
Nonsucking	6	
Perforating		15
Sucking	5	
Nonsucking	10	

Hemothorax was present in all thirty-one fatal cases in amounts varying from 200 to 2,500 cubic centimeters. The increase in mortality with the amount of hemothorax is demonstrated in Table VI.

An attempt is made in Table VII to correlate mortality with severity of injury.

The causes of death are given in Table VIII. Case 5 in Table VIII was interesting enough to deserve special notes. This patient had a penetrating

TABLE VI. RELATION OF VOLUME OF HEMOTHORAX TO MORTALITY

VOLUME OF HEMOTHORAX (C.C.)	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
0 to 500	49	2	4
500 to 1,000	53	3	5.6
1,000 to 1,500	41	5	12
1,500 to 2,000	68	9	13
2,000 to 2,500	78	12	15.4

TABLE VII. EFFECT ON MORTALITY OF INCREASE IN NUMBER OF MAJOR INJURIES

TYPE OF INJURY	NUMBER OF CASES	DEATHS	MORTALITY (PER CENT)
No visceral injury (pulmonary or other) and no major extrathoracic injury	178	4	2.2
One visceral injury	88	7	7.9
Two visceral injuries	13	4	30.0
Three or more visceral injuries	4	2	50.0
Visceral injury without major extrathoracic injury	48	5	10.0
Visceral injury with major extrathoracic injury	43	9	20.0

TABLE VIII. CAUSE OF DEATH

CASE	TIME INTERVAL BETWEEN OPERATION AND DEATH	CAUSE OF DEATH
1	3 hr.	Blast injury to both lungs
2	7 days	Pneumonia both lungs
3	7 days	Delayed hemorrhage from lacerated azygous vein
4	1 day	Blast injury to both lungs
5	3 days	Fibrinous pleuritis
6	8 hr.	Blast injury to lungs
7	1 day	Unknown
8	7 days	Meningitis—patient had cord transection
9	7 days	Severe contusion of lung
10	3 days	Shock
11	Died at operation	Unknown
12	2 hr.	Blast injury to lungs
13	Died at operation	Vagovagal reflex—patient had mediastinotomy
14	1 hr.	Shock—patient bled from lacerated axillary vein
15	7 days	Pneumonia both lungs
16	15 min.	Shock
17	1 hr.	Shock
18	7 hr.	Shock
19	4 days	Crushed lung
20	Died on table	Shock
21	Died on table	Lacerated ventricle
22	Died on table	Intrabronchial hemorrhage
23	1 day	Shock
24	1 day	Compound skull fracture
25	12 hr.	Shock
26	12 hr.	Shock
27	Died on table	Lacerated right ventricle and superior vena cava
28	3 days	Anoxia
29	2 hr.	Shock
30	1 hr.	Shock
31	1 day	Shock

TABLE IX. TIME OF DEATH IN RELATION TO OPERATION

TIME INTERVAL BETWEEN OPERATION AND DEATH	NUMBER OF CASES	MORTALITY (PER CENT)
Died at operation	6	19.3
Zero to twelve hours postoperative	10	32.2
Twelve to twenty-four hours postoperative	6	19.3
Second day postoperative	0	0
Third day postoperative	3	9.4
Fourth day postoperative	1	3.6
Fifth day postoperative	0	0
Sixth day postoperative	0	0
Seventh day postoperative	5	16.2
Totals	31	100.0

sucking wound of the left chest. By x-ray the stomach was shown to be high. However, the patient stated that as a boy he had had a left phrenicectomy for tuberculosis. It was the feeling of the surgeon that the diaphragm was elevated due to the old phrenic crush and that the stomach was below the diaphragm. A débridement and closure of the chest wall wound were done. Postoperatively the patient did poorly and died on the third day. Autopsy revealed a congenital diaphragmatic hernia of the stomach which has been perforated.

Shown in Table IX is the relation of mortality to the interval between operation and death. It will be seen that sixteen patients, or 52 per cent of the cases, died in the first twelve-hour period; of these, ten deaths, or 62 per cent, were attributable to shock. Additional analysis reveals that 71 per cent of those patients who died in the first twenty-four hour period died of shock.

SUMMARY

A series of 374 intrathoracic war wounds with a gross mortality of 8.2 per cent has been presented. The special problems associated with preoperative management of thoracic wounds have been outlined, the operative management considered, and the postoperative care detailed. Finally, the fatal cases have been analyzed from several points of view. Shock proved to be responsible for the majority of fatalities.

REFERENCES

1. Falor, W. H., Jones, H. W., and Burbank, C. B.: 165 Acute Combined Wounds of the Thorax and Abdomen, Ohio State M. J. **42**: 931, 1946.
2. Jones, H. W., Jr., Falor, W. H., and Burbank, C. B.: 524 War Wounds on the Western Front, Bull. Johns Hopkins Hosp. **79**: 283, 1946.

THE SIX SUBPHRENIC SPACES

Applied Anatomy and Surgical Considerations

Philip Thorek, M.D.
Chicago, Ill.
(From The Department of Surgery, University of Illinois, The American and Cook County Hospitals, and The Cook County Graduate School of Medicine)

THIS paper has been titled "The Six Subphrenic Spaces" to emphasize the importance and existence of six distinct anatomic spaces in this region. This, in turn, aids in earlier recognition and treatment of subphrenic infections and abscesses. There are many ways of describing the anatomy of the subphrenic region, but the description must be kept both anatomic and practical.

The frequency of subphrenic involvement was emphasized in a rather exhaustive study by Ochsner and Graves[1] in 1933. They reported and analysed 3,372 cases collected from the literature and their personal cases. If the presence of subphrenic pathology be kept in mind, especially as a complication of intra-abdominal suppurative processes, it can be diagnosed earlier and treated more effectively.

Anatomy.—Martinent,[2] as far back as 1898, accurately described the subphrenic spaces. In 1908, Barnard[3] amplified this description and included the surgical aspects. These studies will be utilized and somewhat modified in the hope that a clear-cut picture of the six anatomic spaces will result.

The subphrenic space per se must be looked upon as that space which exists between the diaphragm above and the transverse colon and its mesocolon below. This area is divided by the liver into supra- and infrahepatic portions. The suprahepatic part is bounded above by the diaphragm and below by the upper surface of the liver. The infrahepatic part is bounded above by the undersurface of the liver and below by the transverse colon and its mesocolon. Three suprahepatic and three infrahepatic spaces exist (Fig. 1). The falciform ligament divides the suprahepatic area into right and left parts. To understand the nomenclature and construction of these spaces, the anatomy of the liver should be reviewed. This can best be done by visualizing cross sections of the right and left lobes of the liver, thereby differentiating the superior from inferior surfaces of this organ. The superior surface of the right lobe of the liver resembles an inverted cup or bowl, so that this surface appears both anteriorly and posteriorly. The cut section of the left lobe, however, resembles a chip so that the dome-shaped anterior and posterior relations of the superior surface are wanting. On the right side, the right lateral ligament which is a prolongation of the coronary ligament divides this area into two spaces, a large anterior and a small posterior one. These ligaments are peritoneal reflections. The left lateral ligament passes along the posterior border of the left lobe of the

Received for publication, July 17, 1946.

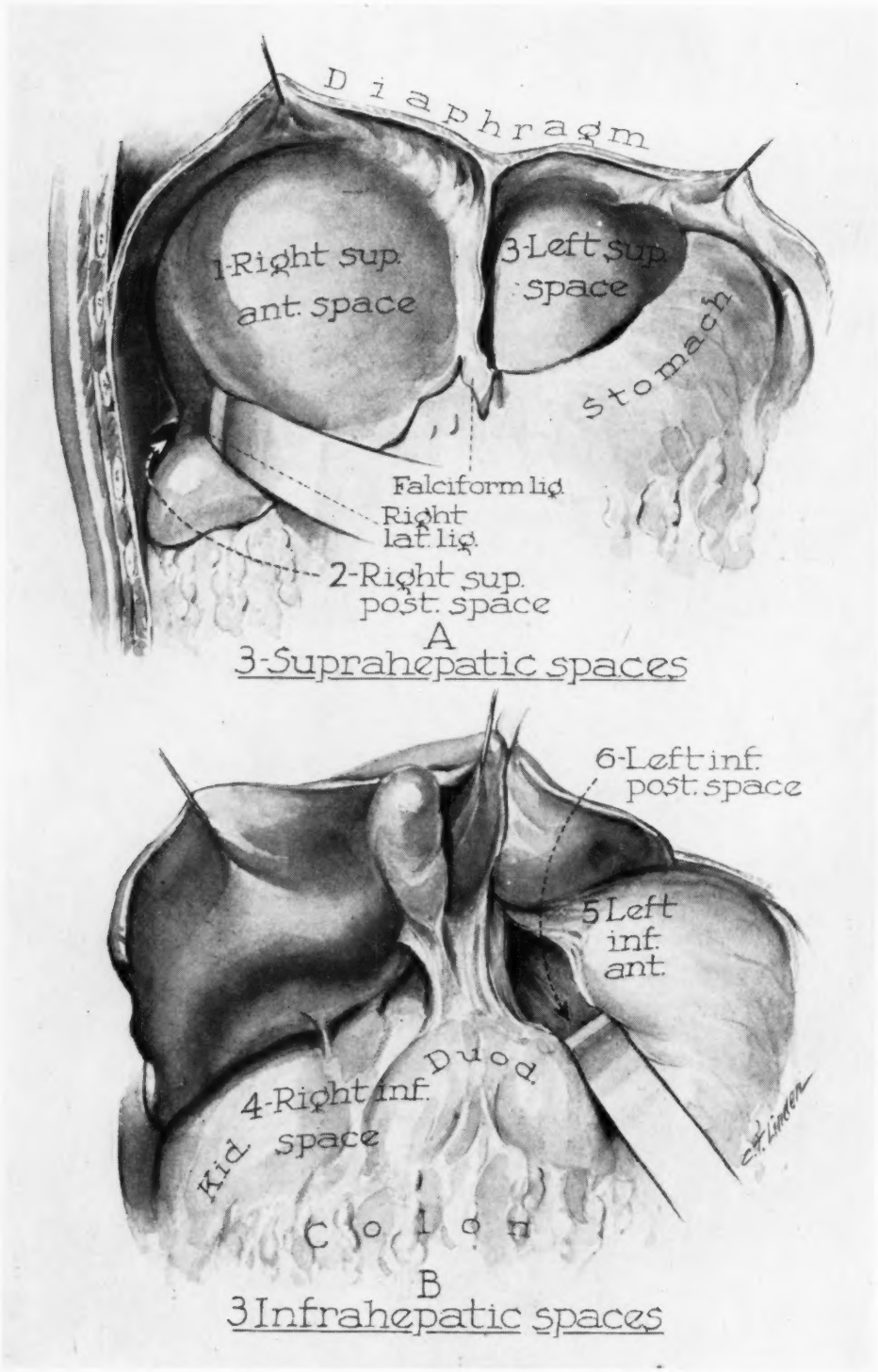


Fig. 1. (*For legend see opposite page.*)

liver and separates the superior from the inferior surface. Therefore, only one space exists to the left of the falciform ligament. The three suprahepatic spaces thus constructed are named in the following way (Fig. 1, *A*): *1*, the space which exists above the liver, anterior to the right lateral ligament and to the right of the falciform ligament, is called the right superior anterior subphrenic space. Space *2* is located to the right of the falciform ligament, takes in the superior surface of the liver, and is behind the right lateral ligament; therefore, it is called the right superior posterior subphrenic space. Space 3 is situated between the liver and the left half of the diaphragm and hence, is known as the left superior subphrenic space.

The infrahepatic area (Fig. 1, *B*) is conveniently divided into right and left parts by the descending portion of the duodenum, although some anatomists use the ductus venosus for this division. To the right of the duodenum and below the liver, the right inferior subphrenic space is located, which is the same as the hepatorenocolic pouch of Morison. The left side of the infrahepatic space is divided by the stomach into anterior and posterior parts. This creates a space which exists to the left of the duodenum and in front of the stomach and hence, is named the left inferior anterior subphrenic space. This also has been referred to as the perigastric space. The final, or sixth space, is situated to the left of the duodenum, below the liver but behind the stomach; it is known as the left inferior posterior space or the lesser peritoneal cavity (omental bursa).

The six spaces are all intraperitoneal, but an extraperitoneal space exists within the confines of the coronary ligament which corresponds to the bare area of the liver. It separates the right superior posterior from the right superior anterior space and is of little clinical importance. Unfortunately, the space most frequently involved is the one which is smallest and most difficult to reach, namely, the right superior posterior. This is due to the fact that the most frequent causes of subphrenic infection are on the right side, namely, acute appendicitis, acute cholecystitis, and perforated peptic ulcer. An inflammatory exudate from any of these three lesions may travel upward along the so-called paracolic groove of the ascending colon and localize in this space, which is the most difficult to reach surgically and the most difficult to diagnose.

The microorganisms most commonly responsible for subphrenic infection or abscesses are the colon bacillus, staphylococcus, and streptococcus. Usually a mixed infection is present. These organisms can gain entrance intraperi-

---

Fig. 1.—*A*, The three suprahepatic spaces. The suprahepatic region is divided by the falciform ligament into right and left parts. Space *1* is situated to the right of the falciform ligament, above the liver and anterior to the right lateral ligament. It is, therefore, called the right superior anterior space. Space *2* is located to the right of the falciform ligament, above the liver and behind the right lateral ligament. It is called the right superior posterior space. Spaces *1* and *2* are separated from each other posteriorly by the bare area of the liver (see Fig. 2, *B*). Space *3* is found to the left of the falciform ligament and since the left lateral ligament passes posteriorly along the flattened left lobe of the liver, there is only one space on this side in contrast to the two on the right. It is called the left superior space.

B, The three infrahepatic spaces. The infrahepatic region is divided by the descending duodenum into right and left parts. For convenience we have numbered these spaces *4*, *5*, and *6*. Space *4* is to the right of the duodenum, and below the liver. It is, therefore, called the right inferior space. This is the same as the hepatorenocolic pouch of Morison. Space *5* is found to the left of the duodenum, below the liver and in front of the stomach. It is called the left inferior anterior space. Space *6* is located to the left of the duodenum, below the liver and behind the stomach. It is called the left inferior posterior space or lesser peritoneal cavity. The arrow indicates its position and surgical approach.

toneally or through vascular channels. Less frequently, however, lesions in the thorax may pass through the diaphragm and into the subphrenic spaces. Intrathoracic involvements are usually complications rather than causes of subphrenic infection. Therefore, a little fluid or involvement of the thorax may mask the clinical picture of the subphrenic pathology and the patient is incorrectly treated for an intrathoracic lesion. Dexter[4] has emphasized the importance of draining a subphrenic abscess before the structures above the diaphragm become involved. This would have a tendency to keep the mortality and morbidity low. Other intrathoracic complications which may make the diagnosis difficult are bronchopleural fistula, lung abscess, and pneumonitis.

All subphrenic infections do not result in subphrenic abscesses. In their analysis, Ochsner and Graves[1] concluded that approximately 30 per cent of subphrenic infections proceeded to suppuration and the remaining 70 per cent subsided spontaneously. It becomes important, therefore, to differentiate diagnostically the nonsuppurative involvement from the true abscess since the therapy of each is different. Almost all subphrenic infections respond to conservative therapy, especially since the advent of modern chemotherapy. This type of treatment, however, will not cure a subphrenic abscess which needs the proper institution of evacuation and drainage.

The diagnosis of subphrenic abscess can usually be made if the condition is kept in mind. The inaccessibility of the subphrenic region also accounts for the delay in diagnosis, but there are many signs and symptoms which will suggest the possibility of this lesion. The onset may be abrupt or insidious, but the one outstanding finding is continuous fever. An unexplained fever which persists following a suppurative intraperitoneal process should at least suggest subphrenic abscess. The patient complains of pain or a sense of pressure in the upper abdomen or loin, which is usually aggravated by deep inspiration and thus may be confused with pleurisy or pneumonia. If an infection is present in the right posterior superior space, the pain may be referred to the lumbar region; however, those cases which involve the right anterior superior space or right inferior space usually have pain which is referred to the right costal margin. Localized tenderness which is found over the involved region is of greatest diagnostic importance, however, its absence does not rule out subphrenic pathology. If an abscess is present in the right posterior superior space, the tenderness localizes over the right twelfth rib. By the same token, local tenderness is found along the costal margin, on their respective sides, in right anterior superior, right inferior, left superior, and

---

Fig. 2.—*A*, Diagrammatic figure to show the skin incision placed over and parallel with the twelfth rib and the deeper transverse incision at the level of the first lumbar spinous process. If this change in position of incisions is kept in mind, the pleural cavity will not be entered.

B, The retroperitoneal approach to an abscess in the right superior posterior subphrenic space. The twelfth rib has been removed and the incision deepened to the peritoneum; the finger peels the peritoneum from the undersurface of the diaphragm until the abscess is entered. This approach avoids both pleural and peritoneal cavities.

C, Incision for drainage of an abscess in the right superior anterior subphrenic space. It is placed below and parallel with the right costal margin and is continued to, but not through, the peritoneum.

D, Approach to a right superior anterior subphrenic space. The finger peels the parietal peritoneum from the undersurface of the diaphragm until the abscess cavity is entered. In this way extraperitoneal drainage is instituted.

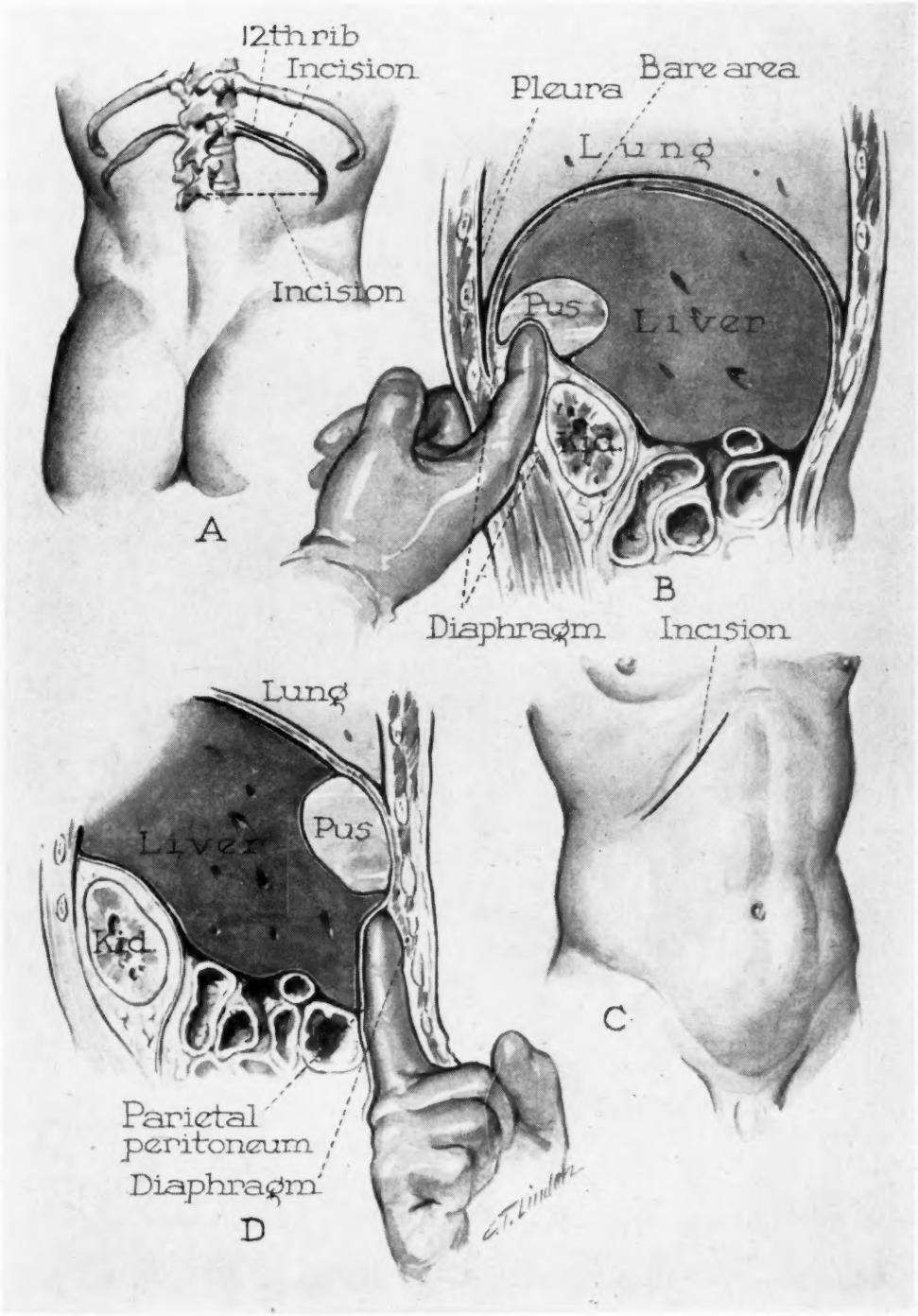


Fig. 2. *(For legend see opposite page.)*

left anterior inferior space abscesses. The liver is displaced downward and an area of increased liver dullness to percussion will be found in involvement of the right anterior superior, right posterior superior, and left superior space abscesses. The x-ray is of great help if one emphasizes the importance of the fluoroscope instead of the x-ray plate. Although it is true that the diaphragm is elevated in subphrenic abscess, this in itself is not pathognomonic. On the other hand, immobility of the hemidiaphragm on the involved side is most suggestive of subphrenic pathology; this sign is of utmost importance and is most essential to the diagnosis. The presence of gas represents a late finding, hence, a neglected case; however, its absence, denoting a more favorable condition, does not eliminate the diagnosis of subphrenic abscess.

The use of aspiration in the diagnosis is feared because of the danger of contaminating the pleural or peritoneal cavities. Many enthusiasts of this method emphasize the fact that this procedure should only be done immediately before operation so that if pus is found, immediate incision and drainage may be instituted; however, we do not share this view.

The treatment is dependent upon the location of the infection and the presence or absence of suppuration. Since the majority of subphrenic infections do not go on to suppuration, these may be treated by conservative measures, especially making use of modern chemotherapy. The clinical course of such a case is carefully watched and charted; if there is no improvement and the white blood count goes over 20,000, this is most suggestive of a suppurative process which will necessitate surgical intervention and drainage. It is of utmost importance to avoid contaminating uninvolved cavities in the drainage of such an abscess. This is imperative where the pleural and peritoneal cavities are concerned, since the marked absorbability of serous membranes might produce an immediate overwhelming toxemia. Ochsner and Graves[1] have divided the surgical approach into either transthoracic or transabdominal, which in turn are divided into transserous and extraserous. The transthoracic extraserous approach can be accomplished by incising below the reflection of the pleura or by mobilizing the costophrenic angle of the pleura upward. The transabdominal extraserous approach (Fig. 2, *C* and *D*) may be accomplished by incising directly over the abscess, if the abscess is extraperitoneally placed, or by mobilizing the parietal peritoneum from the undersurface of the diaphragm and following this to a suprahepatic abscess. If an intraperitoneal abscess exists, in which adhesions between the parietal peritoneum and the abscess are present, the cavity may be drained "extraserously" since the incision is made through the adhesions and the peritoneal cavity remains uncontaminated. The ideal procedure, therefore, is an extraperitoneal one approaching the abscess either from in front or from behind, depending upon the location of the abscess. Since the right superior posterior space is the one most frequently involved, a "retroperitoneal operation" is usually performed (Fig. 2, *A* and *B*). This procedure has been too frequently described to warrant repetition. The only point which bears emphasis, however, is based upon the work of Melnikoff[5] who showed the variations and the relation of the costophrenic angle to the

twelfth rib. Based on this work the skin incision is made along the course of the twelfth rib, but the incision through the rib bed should change its course to a transverse one. The latter is made at the level of the spinous process of the first lumbar vertebra, thus avoiding contamination of the pleural cavity.

CONCLUSIONS

1. Six subphrenic spaces are described.

2. This simplifies the surgical anatomy, diagnosis, and treatment of subphrenic infections.

3. Diagnostic and therapeutic suggestions are presented.

REFERENCES

1. Ochsner, Alton, and Graves, Amos: Subphrenic Abscess, Ann. Surg. **98**: 961, 1933.
2. Martinent, A.: Des varietes anatomiques et d'abces sous phrenique, Thesis in Paris, 1898.
3. Barnard, H. L.: Surgical Aspects of the Subphrenic Abscess, Brit. M. J. **1**: 371, 429, 1908.
4. Dexter, R.: Observations on the Diagnosis of Subphrenic Abscess, Am. J. M. Sc. Vol. **119**: 810, 1925.
5. Melnikoff, A.: Die Chirurgische Anatomie der Sinus Costodiaphragmaticus, Arch. f. klin. Chir. Vol. **123**: 133, 1923.

COTTON VERSUS CATGUT AS SUTURE MATERIAL IN HERNIORRHAPHY

GILSON COLBY ENGEL, M.D.,* AND JOHN C. REGANIS, M.D.,† PHILADELPHIA, PA.

MANY types of suture material have been used in the repair of hernias, always with the idea of decreasing tissue reaction and yet with strength enough to hold until real fibrous healing has taken place.

In discussing suture material we do not ignore the type of hernia or the mechanics of the particular type of repair as these are of paramount importance. We believe that fascia alone as an isolated material does not constitute a good repair unless it is connected with muscle and its function. Muscle must play a part in any hernial repair to have a good permanent result. This is necessary to accommodate for the sudden changes in intra-abdominal pressure such as is seen with coughing, sneezing, and heavy lifting.

After one decides what type of mechanical repair should be done for a particular hernia, the next choice is in the selection of the suture material. We were much impressed with the report by Meade and Ochsner[1] on cotton as a suture material. In March, 1941, we began work on a series of herniorrhaphies repaired with cotton and would now like to report on part of this group in contrast to a like group repaired with catgut.

A later paper by Meade and Ochsner[2] contrasting the relative value of catgut, silk, linen, and cotton as suture material further convinced us of the real value of cotton. They have pointed out that although dry cotton has less tensile strength size-for-size than catgut, silk, or linen, after it has been placed in the tissues it shows much less decrease in tensile strength than the others.

Howes and Harvey[3] showed that there was no need for using a suture material which had greater tensile strength than the tissue in which it was placed. We feel there can be no argument about this and thus see only an occasional use for wire.

Howes[4] found and reported that a wound which is closed with catgut is weakest between the fourth and eighth days due to a considerable decrease in the tensile strength of the catgut and the insufficient lapse of time for the fibroblastic strengthening of the wound. It is only after the eighth day that the wound becomes as strong as the surrounding tissue.

According to the experience of those who have analyzed a large number of wound disruptions, it was found that they usually occur between the fifth and twelfth days and most frequently between the seventh and ninth days. Ries[5] and Fallis[6] reported disruptions with catgut as early as the second day and even then were unable to demonstrate catgut in the wound. The tensile strength of various sutures was studied by Howes[4] and was found to decrease at fourteen

Received for publication, July 25, 1946.

*Professor of Clinical Surgery, Graduate School of Medicine, University of Pennsylvania, and Chief of Surgical Service B, Lankenau Hospital.

†Resident, Surgical Service B, Lankenau Hospital.

days, except that the tensile strength of cotton remained practically unchanged from the original. There was a loss of chromic catgut of 30 per cent in four days, 50 per cent in seven days, and 60 per cent in ten days. A cotton suture No. 50 remaining in human tissue for eighteen days showed only a 10 per cent loss in strength.

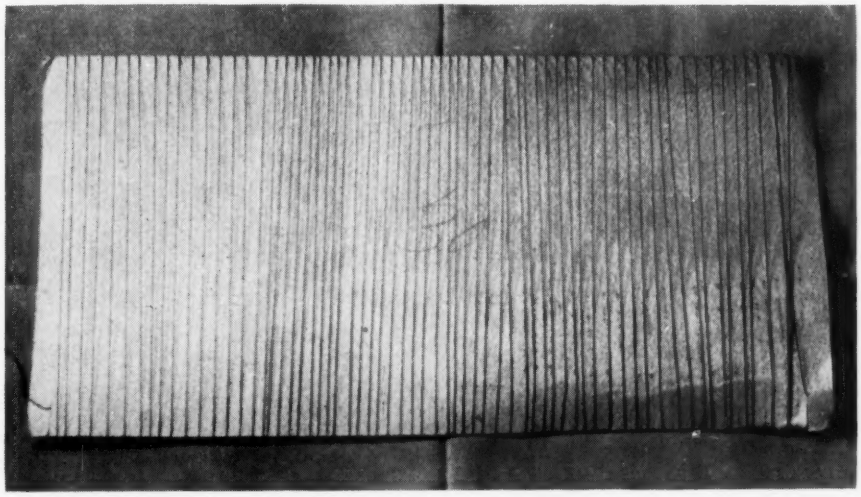


Fig. 1.—Cotton wrapped on cardboard preparatory to its being wrapped in sheet for sterilization. Size of cotton is marked on the cardboard and can be seen as No. 30.

Fig. 2.—The card wrapped in cloth ready for sterilization in the autoclave at twenty pounds' pressure for twenty minutes. This outer cloth is also marked as to the size of the cotton.

Absorbable sutures produce essentially a wet reaction in tissue which is an attempt on the part of the host to digest the sutures by means of proteolytic ferments derived from leucocytes. This wet reaction consists of excessive fluid and cellular exudate which is associated with a delay in the appearance of

fibroblasts. Both of these factors slow wound healing. Nonabsorbable sutures produce a minimum of exudate (dry reaction) with early fibroblastic proliferation. When wounds are closed with cotton the tissue reaction is minimal and fibroblasts appear earlier. Fibroblastic proliferation occurs in five to seven days with catgut and in two days with cotton.

The material we used in this series, and which we are still using, was regular white sewing cotton, sizes 8, 30, and 50.

A cardboard is selected, seven by twelve inches. Along the twelve-inch sides nicks are cut about one-eighth inch apart. The cotton is wound on the cardboard in these nicks. The card wrapped with cotton is then covered with a cloth and labeled as to size. The cardboard is used in sterilization since it bends as the heat contracts the cotton and the threads will not break. The sterilization is done in the autoclave at twenty pounds' pressure for twenty minutes. On removing the card containing the cotton from the sterile cloth the cotton strands are cut in the long axis of the cardboard by the sterile nurse. This produces fourteen-inch lengths of the suture material (Figs. 1 and 2).

The cases selected for this study were taken from the first group of hernias repaired with cotton sutures so that we would have at least a four-year follow-up. The catgut series was selected for about the same period of follow-up. For both catgut and cotton groups we chose primary inguinal hernias; no recurrent hernias were selected in either series.

The age groups were fairly similar and are expressed in Table I.

TABLE I. AGE GROUPS

YEARS	COTTON	CATGUT
12 to 20	12	6
20 to 30	24	26
30 to 40	23	28
40 to 50	22	15
50 to 60	16	18
60 to 70	3	5
70 and upward	0	1

The operations were performed by members of Surgical Service B and the same technique for repair was used in all the cases (Bassini). For suturing the conjoined tendon to the shelving margin of Poupart's ligament, No. 8 cotton was used. The aponeurosis of the external oblique was sutured with No. 30, and No. 50 was used for ligatures.

The incidents of male and female, and right and left inguinal, in the 200 cases are shown in Table II.

No strangulated hernias were included in either group.

The postoperative temperature reactions of cotton and catgut in herniorrhaphy have been described by Zollinger and Flynn.[7] They found that the

TABLE II.

	MALE	FEMALE	RIGHT	LEFT
Cotton (100)	91	9	70	30
Catgut (100)	94	6	60	40

first postoperative day temperature was 99.4° F. with cotton as compared with 100.0° F. with catgut. They further found that a normal average temperature was attained, in cases in which cotton was used, on the fourth postoperative day as compared to the sixth postoperative day for those with catgut.

Our experience shows that the first postoperative day temperature was 99.6° F. with cotton and 99.5° F. with catgut. In both types of cases normal average temperatures were attained on the fourth postoperative day. Thus, we find very little difference in the two groups so far as temperature reaction is concerned.

Far more important than temperature reaction, we believe, is the immediate postoperative condition of the wound and the permanent result of the herniorrhaphy. First, in regard to the appearance of the wound, Shambaugh[8] showed incidents of suppurative wounds to be twice as great following the use of catgut as following silk. The wounds in which cotton was used in our cases showed some reaction (redness) which disappeared on the second postoperative day. Those in which catgut was used showed a reaction not only of redness but of edema and induration persisting until the tenth to fourteenth postoperative day. Our feeling is definitely that cotton gave a much less local reaction than did catgut regardless of the equality of the patients' temperature reactions.

Our study of complications between the cotton and the catgut series confirms this statement. As to wound complications with cotton, we had one case (1 per cent). This patient had a hematoma of the wound, which we believe, was due to faulty technique in not having a dry wound at closure. In the catgut series, however, we had ten cases (10 per cent) with wound complications. Four were infected wounds and six involved serum collections in the wounds. This contrast was the most striking of all in our study and we believe this alone justifies the use of cotton sutures.

Other complications were limited to the respiratory tract, testicle, and urinary bladder. A comparison of cotton and catgut complications is shown in Table III.

TABLE III. COMPLICATIONS IN CATGUT AND COTTON SERIES

CATGUT			COTTON		
NUMBER	COMPLICATION	ANESTHESIA	NUMBER	COMPLICATION	ANESTHESIA
6	Serum collection	Spinal	1	Hematoma	Cyclopropane
4	Wound infections	Spinal	1	Atelectasis	N_2O-Ether
1	Orchitis	Spinal	3	Upper respiratory	Spinal
1	Pleurisy	Spinal	1	Orchitis	Spinal
2	Cystitis	Spinal			

The predominant anesthesia for both groups was spinal, representing 70 per cent of both groups. The other 30 per cent consisted of local and general anesthesia.

As to the permanency of results of the total 200 cases, follow-up studies were done on all of them. These follow-ups represent three- to four-year postoperative checks. In the catgut series there were six recurrences (6 per cent). There were four recurrences in the cotton series (4 per cent). This represents a reduction of recurrences of one-third which is, we believe, significant. Meade

and Long,[9] in a study of 465 consecutive wounds in which cotton suture material was employed, demonstrated cotton to be highly satisfactory in its clinical application. We believe that our work with cotton bears out their findings. For the past six months we have been using cotton suture material in all abdominal operations associated with early ambulation and expect to report on this experience in the near future.

In summary, a review of the literature has been reported regarding cotton as a suture material.

We have presented a contrast study of 100 consecutive uncomplicated inguinal hernias repaired with cotton and 100 consecutive uncomplicated inguinal hernias repaired with catgut.

The same type operation was done in all cases in both groups (Bassini).

All of the operations were done by members of Surgical Service B staff.

In conclusion, our findings substantiated the findings of other workers favoring cotton as a suture material.

There was less tissue reaction in the wounds sutured with cotton.

There was no difference in temperature reaction in the two groups.

There were fewer wound complications with cotton sutures.

The recurrence rate was reduced one-third in the cotton series.

REFERENCES

1. Meade, W. H., and Ochsner, A.: Spool Cotton as a Suture Material, J. A. M. A. **113**: 2230, 1939.
2. Meade, W. H., and Ochsner, A.: Relative Value of Catgut, Silk, Linen, and Cotton as Suture Materials, SURGERY **7**: 485-514, 1940.
3. Howes, E. L., and Harvey, S. C.: Tissue Response to Catgut Absorption, Silk, and Wound Healing, Internat. J. Med. & Surg. **43**: 225-230, 1930.
4. Howes, E. L.: The Strength of Wounds Sutured With Catgut and Silk, Surg., Gynec. & Obst. **57**: 309, 1933.
5. Ries, Emil: On Postoperative Separation of Laparotomy Wounds, Am. J. Obst. & Gynec. **60**: 569, 1909.
6. Fallis, L. S.: Postoperative Wound Separation: Review of Cases, SURGERY **1**: 523, 1937.
7. Zollinger, Richard W., and Flynn, Wm. J.: The Effect of Cotton and Catgut in Hernial Repair on Postoperative Temperature and Pain, Surg., Gynec. & Obst. **81**: 201-205, 1945.
8. Shambaugh, P.: Postoperative Wound Complications. A Clinical Study With Special Reference to Use of Silk, Surg., Gynec. & Obst. **64**: 765, 1937.
9. Meade, W. H., and Long, C. H.: Use of Cotton as Suture Material, With Particular Reference to Its Clinical Application, J. A. M. A. **117**: 2140-2143, 1941.

DISLOCATION AT THE ACROMIOCLAVICULAR ARTICULATION

A Note on Technique of Radiographic Examination of the Shoulder in Suspected Dislocation at the Acromioclavicular or Humeroscapular Articulation

Lieutenant Colonel Charles J. Sutro, Medical Corps,
Army of the United States

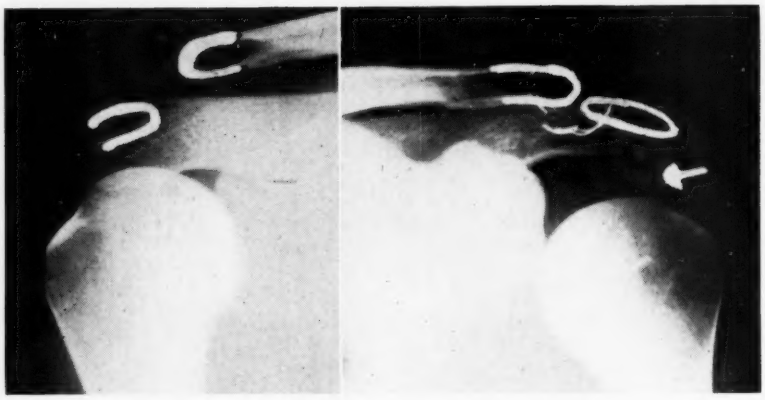
ON NUMEROUS occasions we have noted on physical examination the existence of a dislocation at the acromioclavicular articulation and the absence of such findings on simultaneous radiographic examination of the part. This was noted especially when the radiographic examination was made with the patient in the recumbent position. On further investigation we observed that in a fresh dislocation at this joint, there is a tendency for the clavicle to realign itself into a normal relationship with the acromium when the patient is in a recumbent supine attitude.[1-5] Similarly, radiographic examination of the shoulder taken in the recumbent position has failed to demonstrate a coexisting partial subluxation of the humeral head* (Fig. 1). For this reason we have added the following technique for the radiographic examination of the shoulder area. The patient stands or sits for two or three minutes with the unsupported affected upper extremity held at the side of the body or chair. A five- to ten-pound weight is then placed in the hand of the affected extremity in order to permit gravity traction to the shoulder area. During a three-minute period of such traction, radiographic examinations are made of the shoulder in the anteroposterior projection with the arm in external and internal rotation and the chest in a neutral as well as in a 15 degree oblique attitude (Fig. 2). These views permit visualization of the humeroscapular joint space and of the subchondral regions of the acromioclavicular articulation.†

A brace was used in the treatment of recent subluxations at the acromioclavicular articulation (Fig. 3). The double straps which extended over the acromioclavicular articulation permitted easy correction of the upward elevation of the acromial end of the clavicle (Fig. 4). The position of the platform for the upper extremity could be readily modified so as to alter the angle of abduction both in the sagittal and coronal planes.[6-9] This brace was worn from six to eight weeks and was applied in the treatment of fourteen patients with excellent results. No surgical intervention was necessary.

Received for publication, June 20, 1946.

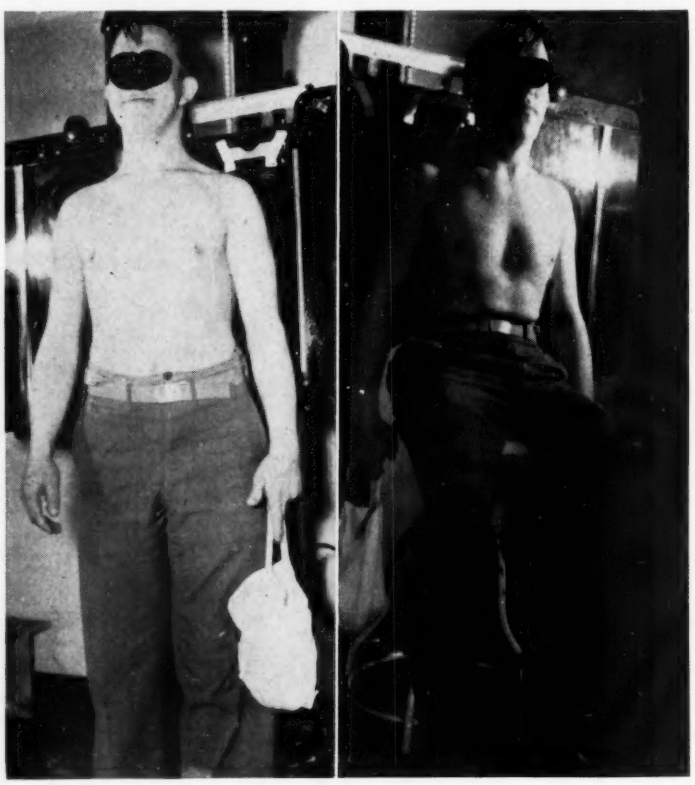
*A patient who was treated at another hospital for a dislocation at the acromioclavicular articulation by surgical intervention complained of pains in the same shoulder. The clinical examination of this area revealed a well-healed scar and a fair range of active and passive motion at the affected shoulder. Radiographic examination disclosed good alignment of the acromium to the clavicle, the presence of wire sutures, and slight irregularity in the subchondral region of these two bones. After two minutes of suspension traction of five pounds to the affected upper extremity, an incomplete subluxation of the ipsilateral humeral head was noted on radiographic examination (Fig. 1).

†In the oblique view one was able to detect a small area of destruction in the acromium as the result of an infection. The other views failed to demonstrate its presence.



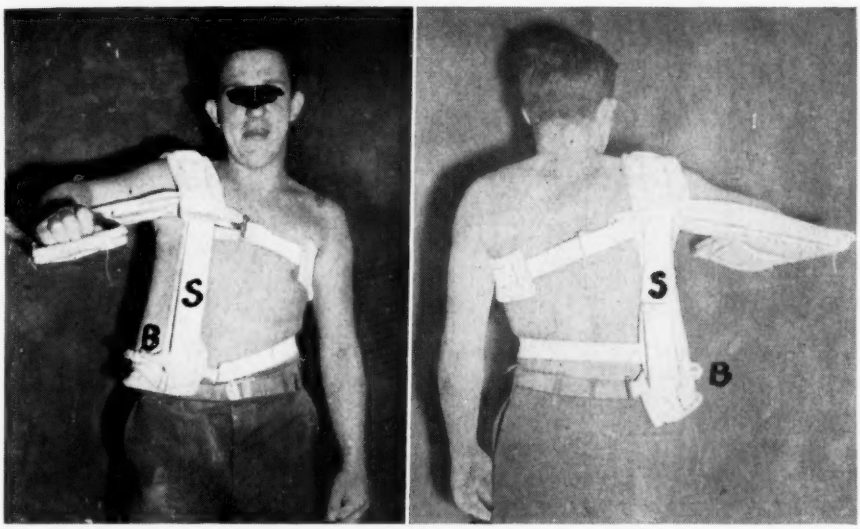
A. *B.*

Fig. 1.—Radiograph (retouched) of the shoulder taken with the patient in a standing attitude with ten pounds of gravity traction to the affected upper extremity. *A*, Note the dislocation at the acromioclavicular joint. In radiographic studies made in the recumbent position, no dislocation was observed in this articulation. *B*, In another patient who was treated for a dislocation at the acromioclavicular articulation, gravity traction to the upper extremity revealed a downward partial luxation of the humeral head (see footnote page 751).



A. *B.*

Fig. 2.—*A* and *B*, Photographs show the method of applying traction to the upper extremity in the standing and sitting attitudes.



A. *B.*

Fig. 3 *A* and *B*.—Photographs show brace from front and back views.

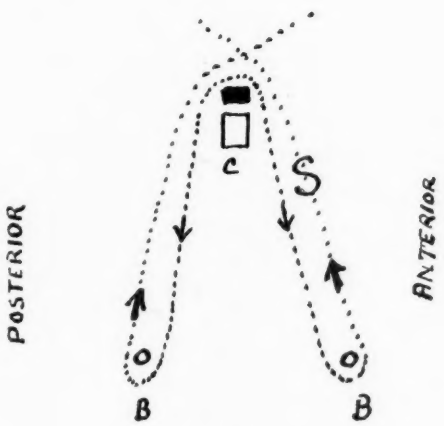


Fig. 3*C*.

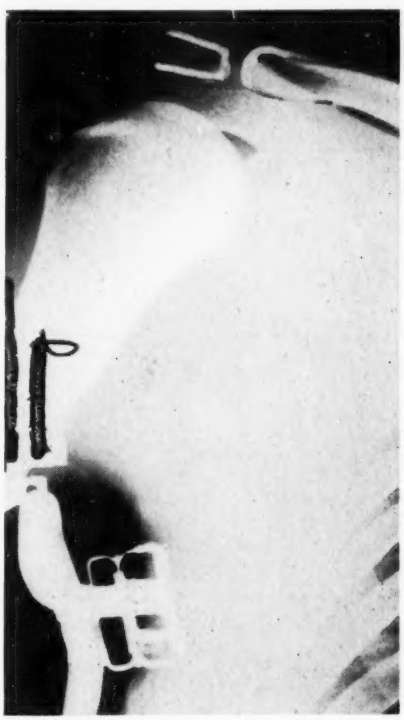


Fig. 4.

Fig. 3 *C*.—Diagram shows the direction of the forces that the double web strap (*S*) exerts on the clavicle (*C*). The black rectangle over (*C*) is a piece of heavy felt. (*B*) is the metal rod on the brace. See Fig. 3, *A* and *B*.

Fig. 4.—Radiograph (retouched) reveals normal alignment of the clavicle to the acromium. The dislocation as noted in Fig. 1, *A* was corrected by the brace.

CONCLUSION

It is suggested that the radiographic examination of the shoulder be made with the patient in a standing or sitting attitude. The affected unsupported arm should be given gravity traction by holding a five- to ten-pound weight in the hand for two or three minutes. By this technique one can readily detect incomplete and complete separations at the acromioclavicular joint. In certain instances, this method has revealed a partial downward subluxation of the humeral head when other examinations have failed to demonstrate any abnormality.

For treatment of dislocation at the acromioclavicular articulation, we have used a brace which readily corrects the elevation of the acromial end of the clavicle.

REFERENCES

1. Pearson, G. R.: Radiographic Technic for Acromioclavicular Dislocation, Radiology **27**: 239, 1936.
2. Shands, A. R., Jr., and Raney, R. B.: Handbook of Orthopaedic Surgery, St. Louis, 1937, The C. V. Mosby Company.
3. Liberson, F.: Value and Limitation of Oblique View as Compared With Ordinary Anteroposterior Exposure of Shoulder; Report of Use of Oblique View in 1,800 Cases, Am. J. Roentgenol. **37**: 498-509, 1937.
4. Holmblad, E. C.: X-ray Examination of Clavicles and Acromioclavicular Joints, Am. J. Surg. **42**: 791-797, 1938.
5. Axen, O.: Ueber den Wert der Arthrographie des Schultergelenkes, Acta radiol. **22**: 268-276, 1941.
6. Trynin, A. H.: The Conservative Treatment of Incomplete Dislocation of the Acromioclavicular Joint, J. Bone & Joint Surg. **14**: 421-424, 1932.
7. Bohler, L.: The Treatment of Fractures, Baltimore, 1936, William Wood & Company.
8. Hart, V. L.: Treatment of Acute Acromioclavicular Dislocation, J. Bone & Joint Surg. **23**: 175-176, 1941.
9. Wolin, I.: Acute Acromioclavicular Dislocation, J. Bone & Joint Surg. **26**: 589-592, 1944.

TRACHEOTOMY IN MAXILLOFACIAL SURGERY

MAJOR GEORGE A. FRIEDMAN, MEDICAL CORPS, ARMY OF THE UNITED STATES

SEVERE maxillofacial wounds are often associated with other injuries. Associated neck injury is especially important in this connection. These extensive injuries tax the combined judgment of the plastic and the oral surgeon, and the anesthetist. Three questions must be answered immediately: (1) How much can we do? (2) How much shall we do? (3) How best shall this be done?

Complete and proper preoperative diagnosis, including over-all evaluation of the injury, answers the first question. The patient's general condition may preclude anything but the most minor repair, even where there is extensive maxillofacial injury. There may be serious intracranial, abdominal, or thoracic complication, which may take precedence in operative importance and priority. Because of a military situation, the patient may arrive in the operating room hours after the original injury was sustained. The facial tissues may be full of debris, clothing, or dirt. The removal of certain fragments, such as those impinging upon the facial nerve, may inflict more harm than their presence.

A mental picture and understanding of the follow-up treatment necessary answer the second question. It may be feasible, in certain cases, not to attempt removal of a foreign body, even when it is lodged in the pharynx. Shall the wound be closed by primary suture? Shall a graft be attempted as primary treatment in a forward hospital with all things considered? Shall tracheotomy be done? Each case may be judged on its own merit.

The indicated anesthesia answers the third question. General anesthesia may be necessary in wounds involving the buccal cavity, pharynx, larynx, and in many cases extensive soft tissue wounds. Pentothal anesthesia is contraindicated in these cases where the aspiration of blood, teeth, mucus, or debris must be prevented. Endotracheal anesthesia is the method of choice, because it provides a free airway, a packed-off larynx, and freedom in the field of operation. Smooth anesthesia enables the surgeon relaxedly to accomplish more in less time, without hurry. The anesthetist must be skilled in the technique of intubation. Trendelenburg[7] first used this method of anesthesia in 1869, already having ascertained the value of a packed-off pharynx in operations around the oral cavity. Before operation tracheotomy was performed and the administration of the anesthetic continued by means of a cannula surrounded by an inflatable cuff inserted into the trachea through the wound. McEwen,[8] a surgeon in Glasgow, introduced the present type of endotracheal anesthesia for operations on tumors at the base of the tongue. Chevalier Jackson, in 1913, described laryngoscopy and the impetus given to this form of anesthesia during the last war made endotracheal anesthesia the method of choice, wherever bleeding into the air passage was a possibility.

Received for publication, May 28, 1946.

The first-aid and preoperative management of these cases is designed generally and primarily toward saving the life of the patient. An airway must be maintained and hemorrhage controlled. Shock treatment is instituted and the patient made as comfortable as possible by splinting and bandaging. The administration of tetanus toxoid or other necessary medication is carried out. The neurosurgeon routinely examines these patients to eliminate the possibility of the presence of intracranial involvement. Other injuries, whether orthopedic, thoracic, or abdominal, are diagnosed for relative importance in relationship to the maxillofacial situation. This cooperative diagnostic effort has made possible a mortality of two maxillofacial cases at this hospital out of a series of several hundred. If possible, and the patient can be turned, roentgenologic study includes views in the lateral, posteroanterior, and occipitomental planes. Three views have proved of definite value in the diagnosis of these cases. The oral surgeon examines the patient and ascertains the amount of dental involvement and, in concert, a combined plan of operation is decided upon. After premedication, the patient is taken to the operating room.

Indications for tracheotomy are as follows: (1) Acute respiratory obstruction is already present, which cannot be relieved by other means. (2) Respiratory obstruction is not yet present, but may occur either during or after operation.

The causes for acute respiratory obstruction are:[8]

1. Falling back of the tongue, which may occur in unconsciousness or in certain mandibular fractures. The tongue acts as a check valve according to Chevalier Jackson, at the laryngeal opening. It is forced by each respiration after which it immediately falls back into its gravity position. Attempts at inspiration draw it over the laryngeal entrance and obstruct the ingress of air. Relief may be obtained by holding the jaw forward and so carrying the tongue away from the laryngeal opening.

2. Foreign bodies over the laryngeal aperture. Their removal is necessary under direct vision because in these cases where they become impacted in the pharynx, death may ensue before they are removed. In some cases, tracheotomy is necessary.

3. Edema of the aryepiglottic folds due to the spread of infection from neighboring structures. This condition may exist preoperatively but may also be a postoperative complication as the result of the spread of inflammation.

4. Adduction of the vocal cords caused by anoxial spasm of the laryngeal muscles. The muscles which adduct and abduct the cords, like all other muscles, work smoothly only when their oxygen supply is adequate. It is likely to occur in unpremedicated anesthetic-resistant individuals. At low levels of oxygen tension, anoxemic spasm of some muscle groups may occur. Spasm may also occur from attempts to intubate the uncocainized larynx under light pentothal anesthesia. The respiratory center is already depressed and the spasm may cause acute respiratory obstruction. This condition may be relieved by the administration of oxygen.

5. Hemorrhage into the air passage, which may cause acute obstruction unless controlled.

6. Direct or indirect injury to any segment of the upper respiratory tract.

The signs of acute respiratory obstruction are:

1. Extreme dyspnea, because respiratory movements have ceased to be effective even though they may continue for a few seconds.

2. The use of the accessory muscles of respiration with an indrawing of the suprasternal and supraclavicular notches.

3. Cyanosis and extreme congestion of the face because the veins at the root of the neck are constricted.

4. Increase of venous engorgement, although the heart continues to beat for some minutes after respiration has ceased, because blood is forced into the vessels, but its return to the heart is not aided by the pumplike mechanism of the thorax.

In war surgery, we are primarily concerned with indications for tracheotomy, where respiratory obstruction is not yet present but the diagnosis leads us to believe that it shall ensue. Respiratory obstruction may arise in some of the following categories:

1. Injuries to the base of the tongue, pharynx, or larynx, with or without the presence of foreign bodies.

2. Large foreign bodies in the air passages where they cannot be removed under direct vision.

3. Extensive soft tissue wounds of the face which may cause later destruction by the spread of inflammation to the mucous membranes of the air passages.

4. Extensive fractures of the mandible where the tongue cannot be held forward by mechanical means.

5. Extensive injury to the *upper* facial regions, especially when these close off completely the nasal passage; or in severe fractures of several of the upper facial elements. Postoperative inflammation may *descend* to involve the pharynx and subsequently the mucous membranes of the air passages.

6. Injury to the recurrent laryngeal or the vagus nerves by direct trauma or by pressure from hemorrhage may cause paralysis of both cords if bilateral and extreme dyspnea may ensue.

7. Surgical emphysema and parapharyngeal infection may occur as sequelae of penetrating wounds of the neck according to Bailey.[1] The former is likely to occur when there is unrelieved laryngeal obstruction, and forced inspiration sucks air into the fascial layers with distention of the tissues. If air enters the mediastinum, respiratory embarrassment ensues which must be relieved by tracheotomy. Parapharyngeal infection, when it occurs, must be opened by a vertical incision over the sternal insertion of the sternocleidomastoid. Tracheotomy may also be necessary.

Gray's[4] *Description of the Anatomy of the Trachea.*—The trachea extends from the cricoid cartilage at the level of the sixth cervical vertebra to its bifurcation into two bronchi, at the level between the sixth and eighth thoracic vertebrae. In the adult, it is a cartilaginous and membranous tube not quite cylindrical, four to five inches long, and approximately one-half its length is

above the sternum. The anterior two-thirds of the tracheal circumference is formed by each cartilage, which is deficient posteriorly where the tube is composed of fibrous tissue and smooth muscle.

The mucous membrane of the trachea is continuous above with that of the larynx and below with that of the bronchi. The submucous layer is composed of a loose meshwork of connective tissue containing large blood vessels, nerves, and mucous glands; the ducts of the latter pierce the overlying layers and open on the surface.

The inferior thyroid arteries supply blood to the trachea with its veins ending in the thyroid venous plexus. The nerves are derived from the vagus and the recurrent nerves and the sympathetic; they are distributed to the tracheal muscles and between the epithelial cells.

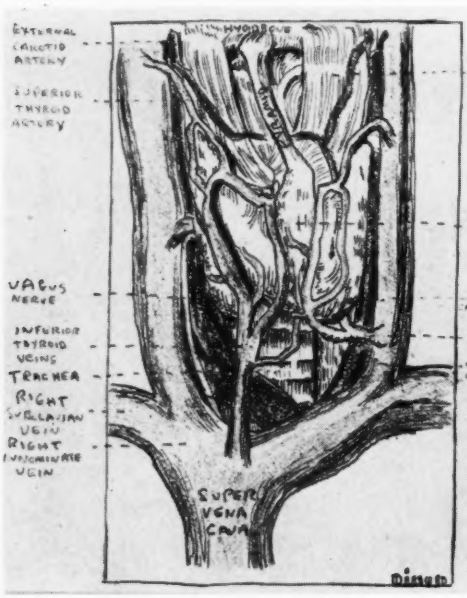


Fig. 1.

Fig. 2.

Fig. 1.—Relations of thyroid gland and trachea (after Gray's Anatomy[4]).
Fig. 2.—Relations of trachea (after Gray's Anatomy[4]).

The surface landmarks and anatomic relations of the trachea are presented in Figs. 1, 2, and 3. Note that the isthmus of the thyroid gland covers the second, third, and fourth tracheal rings anteriorly; that laterally the trachea is in relation with the common carotid arteries, right and left lobes of the thyroid gland, inferior thyroid arteries, and recurrent nerves.

Operation.—The operation of choice in children has generally been described as *high tracheotomy* where the tube is inserted *above* the isthmus of the thyroid gland. This approach avoids the thymus, but carries with it the danger of chronic laryngeal stenosis. *Low tracheotomy* is done with the point of entrance *below* the isthmus of the thyroid gland. The fifth cartilaginous ring, including the one above or below, is the ideal point of entrance for the tracheotomy tube.

The trachea is more deeply placed as it descends and also below this point larger blood vessels may be encountered. Orderly and planned tracheotomy, where time is at hand, is carried out under local anesthesia.

The position of the patient is extremely important. A pillow or sandbag is placed under the shoulders and the head is thus extended. The trachea is thus brought forward closer to the operative field and is fixed.

The operative field is made sterile. The midline of the neck is palpated, the position of the thyroid and the cricoid cartilages rapidly ascertained, and the position of the thyroid isthmus found. The skin is infiltrated with 2 per cent procaine with eight minims of epinephrine to the ounce. The subcutaneous structures are also infiltrated.

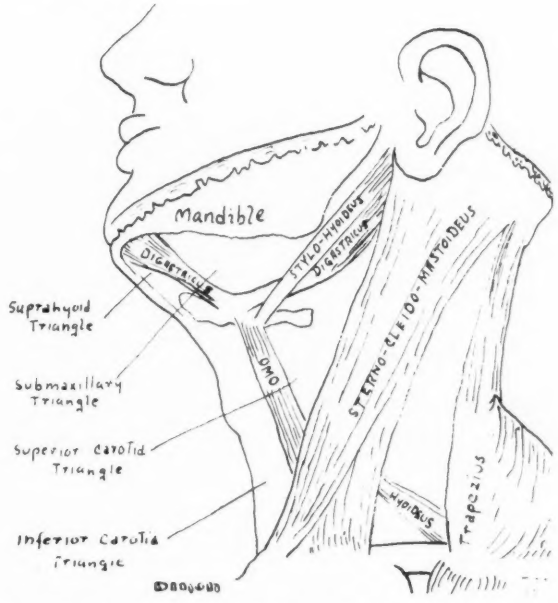


Fig. 3.—Triangles of neck showing the inferior carotid triangle in which tracheotomy is performed.

A horizontal[3] incision is made, one inch long, equidistant from the midline just below the level of the thyroid isthmus. The horizontal incision is the natural incision in all operations on the neck. Experience has shown that these operations heal more satisfactorily than where the vertical incision has been made. In emergency tracheotomy where time is at premium, a vertical incision may be permissible. After the skin incision, exactly in the midline, a *vertical* incision is made into the fascia. If necessary, more anesthetic can be infiltrated into subcutaneous tissues. In healing, the subcutaneous reapproximation in one plane, and the skin in another, produces a wound exactly the size of the tracheotomy tube. Bleeding is a prominent feature of the operation and is due largely to the engorgement of the tissues because of the resistance to the venous return to the thorax. All bleeding vessels are retracted laterally, and if the thyroid isthmus happens to be in the field of

operation, it is retracted upward, but if the original incision was made properly, this will not be necessary. The pretracheal fascia is incised, and the trachea is recognized as a glistening, pink, longitudinal structure. With the trachea under direct vision, a vertical incision is made upward into the anterior surface. The trachea must not be separated from its surrounding structures since this shall interfere with its blood supply.[3] A suction apparatus may be needed when the trachea is opened and is to be held in readiness. A small amount of procaine may be injected into the tracheal wall and lumen. Cocaine has been suggested, but we have had no experience with it. A perfectly dry field is desirable and blood should not get into the trachea. The incision into the trachea is made in an upward direction to avoid cutting too deeply into the trachea and possibly injuring the esophagus. If conditions are favorable, a small oval window is made in the trachea, since this precludes pressure on the tracheal wall and there may be sloughing of cartilage pressed against the tube. The tube is guided with care into the aperture which is spread by a tracheal retractor, by means of an introducer. It is easy to place the tube either to the front or to the side of the trachea. After the tube is in position the introducer is withdrawn and the inner tube is inserted. The stimulus of opening the trachea may cause a bout of coughing, which may expel mucus or start bleeding. The suction apparatus draws off any accumulation of mucus. If there is prolonged bleeding it is necessary to ligate the vessel. The field should be absolutely dry before the patient leaves the operating room. If at any time respiration ceases, artificial respiration is started. If the original incision has been made properly, no suturing of the skin should be necessary; however, one or two sutures may approximate the lateral boundaries of the original incision. Petrolatum gauze is placed between the tube and the skin with the former fixed into position by tapes tied around the patient's neck. A layer of moistened gauze is placed over the front of the opening to prevent the inhalation of dust or foreign bodies. As an additional precaution, an additional tube and inner tube are tied around the patient's neck in the event that the first become clogged or dislodged by an explosive cough.

There are immediate dangers to the operation, which must be avoided. The operator must adhere to the midline of the neck, or the great vessels may be incised. Incision into the esophagus causes a fistula with subsequent mediastinitis and possibly fatality. There is the removed risk of stenosis, following operation, if the incision is made too high.[5] Chevalier Jackson reported that five-sixths of his cases of chronic laryngeal stenosis, in the past thirty years, have been due to faulty tracheotomy or improper aftercare of the tracheotomy tube and wound. After emergency tracheotomy, sometimes performed without anesthesia, which involves the first ring of the trachea or the cricoid cartilage, it may be feasible to perform a secondary tracheotomy lower down to diminish the risk of stenosis.

Aftercare.—The tracheotomized patient should never be separated from a suction machine until he reacts, if general anesthesia has followed. This patient should never be left alone until he becomes cooperative and is able to

take care of himself. He is instructed in the use, care, and function of the tube. This must not be allowed to become clogged by secretions, and it is suctioned out at regular intervals. The outer tube is changed daily to prevent ulceration and secondary hemorrhage. The gauze over the opening is kept in place. The ribbon should never be cut unless a medical officer or trained personnel are present. Sedatives and narcotics are used as sparingly as possible postoperatively, since the cough reflex is an important protective mechanism in preventing the accumulation of bronchial secretion.

CASE REPORTS

CASE 1.—J. B. was admitted to a field hospital in France, July 13, 1944. He had suffered an extensive gutter type, perforating through-and-through wound of the soft tissues of the right cheek. The shell fragment had caused some loss of tissue, but there was no bone involvement. Respiration seemed normal and the airway patent. Since there was no evidence of any respiratory obstruction, a tracheotomy was not performed.

Under pentothal anesthesia for induction, the anesthetist attempted to intubate the patient for endotracheal anesthesia. There was difficulty in getting the tube into the larynx and the patient developed respiratory difficulty during the procedure. The intubation which was attempted under barbiturate anesthesia caused a laryngeal spasm. The respiratory center was already depressed and the administration of the anesthetic caused anoxemic spasm of the adductor muscles of the larynx.

In this case preliminary tracheotomy might have saved the patient's life because inflammation which descended from above caused swelling of the aryepiglottic folds. The intubation caused the larynx to go into a spasm which could not be relieved. A tracheotomy would have prevented this additional trauma to the respiratory tract.

CASE 2.—A. P. was admitted to a field hospital in France, July 15, 1944. He had suffered a severe gunshot wound of the mandible. The wound of entrance was at the left angle of the mandible and the missile coursed along the base of the tongue, lacerating it as well as the left posterior tonsillar pillar. The bullet had traversed the buccal cavity from the left to the right and lodged itself in the tissues of the right cheek. Examination revealed an extensive laceration of the tongue and edema of the aryepiglottic folds. X-ray examination showed a complete, compound, comminuted fracture of the right ramus of the mandible.

Operation.—Horizontal tracheotomy was performed under local anesthesia. Nitrous oxide-oxygen ether was administered endotracheally through the tracheotomy tube as in Fig. 4 and the larynx packed. The lacerations of the tongue and left tonsillar pillar were sutured and the bullet was removed from the right cheek intraorally. The right buccal mucous membrane was approximated. The wound of entrance was débrided minimally and closed by primary suture. A rubber drain was inserted under the inferior border of the right angle of the mandible up to the fractured area. The fractured mandible was fixed by means of intermaxillary continuous loop wiring with intramaxillary elastics.

The patient had an uneventful postoperative course and was evacuated to the zone of the interior. The tracheotomy was the key to the ease with which the situation was handled.

CASE 3.—S. F. was admitted to a field hospital in France, July 16, 1944. The patient had received multiple, severe shell wounds which had penetrated the face and neck. He was suffering from marked dyspnea upon admission with obvious respiratory obstruction. This was caused by a concomitant esophageal injury and the tentative diagnosis was tracheoesophageal fistula. The indication for tracheotomy was self-evident because of the marked dyspnea in connection with a trauma to the neck.

Operation.—Horizontal tracheotomy was performed under local anesthesia. There was a continuous escape of brownish intestinal contents through the tracheotomy tube which confirmed the diagnosis of tracheoesophageal fistula. Gastrostomy to divert the intestinal contents as a preliminary was decided upon before attempted repair of the fistula. The patient's condition became steadily worse and he died even before this was done.

Two other patients with tracheoesophageal fistula came under our observation. In both of these cases the patients died before operative interference.

Fig. 4 (Case 2).—An example of extensive facial injury. Anesthesia is being given endotracheally by means of a tube extending into the tracheotomy tube. Anesthesia was given this way in Case 4 also.

CASE 4.—B. W. was admitted to a field hospital in France, July 22, 1944. He had suffered multiple shell wounds of the perforating type which caused the following: fracture compound, comminuted of the right and left frontal sinuses, orbits, malar-zygomatic compounds, maxillary antra, nasal bones, and maxillary frontal processes. There was maceration of the right and left eyes.

Tracheotomy was indicated although the upper facial elements were involved because the severity of the injury would have made the maintenance of a normal airway impossible postoperatively. The operation itself could not have been performed without it. Thus, a tracheotomy was performed under local anesthesia and the anesthetic administered through the tube (as in Case 2 and illustrated in Fig. 4). The frontal sinuses were irrigated, mucous membranes exenterated, and drainage established to the outside. By means of the Caldwell-Luc approach on both sides, the mucous membranes of both maxillary antra were exenterated. The maxillary elements were elevated and repositioned and both antra packed with petrolatum gauze. Drainage was thus established from above into each

superior gingivolabial sulcus. The maxilla was wired by means of continuous loop wiring and splinted upward by bandaging and pulling up of the mandible.

The postoperative course was uneventful and the patient was evacuated to the zone of the interior.

CASE 5.—B. H. was admitted to an evacuation hospital in France, Aug. 15, 1944. He had suffered a severe gunshot wound which had perforated the neck. There was a massive hematoma on the left side of the neck. He had marked dyspnea due to the pressure on the recurrent nerves or the vagus.

The indication for tracheotomy was present and it was performed under local anesthesia. The hematoma was drained to the outside.

The patient was given supportive therapy. His condition improved and he was evacuated.

CASE 6.—E. C. was admitted to an evacuation hospital in France, Aug. 25, 1944. There was a severe perforating gunshot wound of the neck with laceration of the common carotid artery. The patient's condition was critical upon admission.

Horizontal tracheotomy was performed under local anesthesia which relieved the patient's dyspnea. The common carotid was ligated under general anesthesia. The patient died twelve hours after operation.

Fig. 5 (Case 7).—Preoperative view of patient showing extensive soft tissue involvement of right cheek and upper lip.

CASE 7.—C. M. was admitted to an evacuation hospital in Holland, Oct. 4, 1944. He had suffered extensive facial injury as shown in Fig. 5. The following diagnosis was made: There were compound, comminuted, complete fractures bilateral of the mandible and of the right maxilla. The wound of the right cheek was extensive, of the gutter type, and

extended into the upper lip where there was a loss of tissue. The tongue was severely lacerated. There were, in addition, a lacerated wound of the scalp and a penetrating wound of the left groin.

Tracheotomy was indicated because respiratory obstruction would have developed although not present. It was performed under local anesthetics and the anesthesia administered through the tube. The lacerations of the tongue were sutured. The maxilla was wired by the dental surgeon by means of continuous loop wires. Arch bars were wired

Fig. 6 (Case 7).—Postoperative appearance of patient on operating table; note tracheotomy tube.

to the teeth of the mandible. Fixation of the mandible to the maxilla by means of intramaxillary elastic traction was effected after the patient recovered from the anesthetic. The dental work was performed in this sequence so that there would be no interference with the suturing of the soft tissues of the face. The facial wound was débrided as conservatively as possible and the wound closed by primary suture. The upper lip was grafted by means of full-thickness skin taken from behind the ear (Fig. 6). The scalp and groin wounds were cared for. A transfusion of 1,000 c.c. of stored blood was given the patient during operation.

The postoperative course was uneventful. He received an additional 500 c.c. of blood and the same amount of plasma. The graft and wound were in good condition when the patient was evacuated after five days of hospitalization in good condition.

CASE 8.—R. W. was admitted to an evacuation hospital in Holland, Oct. 7, 1944. He had suffered a severe perforating wound of the face with complete loss of outer nose as well as the bony and cartilaginous nasal elements (Fig. 7). There was skin loss of the upper lip as well as of the symphysis of the mandible. The maxilla was fractured on both sides. The patient seemed to have a patent airway and it did not seem necessary to perform tracheotomy.

Intubation was through the mouth and endotracheal anesthetic was administered. The wound area was débrided and bilateral intranasal antrostomy performed for the drainage of both maxillary antra. The outside skin was approximated to underlying mucous membrane circumferentially. Fixation was accomplished (as in Case 7).

Fig. 7 (Case 8).—Loss of nasal elements and loss of skin over symphysis of mandible; tracheotomy was necessary in this case postoperatively.

Forty-eight hours after operation the patient was observed to be experiencing difficulty in breathing. There was probably a combination of inflammation as well as mechanical interference, because of the packing of the nasal area and the fixation.

Horizontal tracheotomy was performed the same day under local anesthesia. The patient did well and was later evacuated in good condition. This is another example for the necessity of tracheotomy when the upper facial elements are involved.

CASE 9.—R. J. was admitted to an evacuation hospital in Holland, Oct. 22, 1944. He had multiple penetrating shell wounds. There were severe wounds on the right cheek and ear. There was a penetrating wound of the neck posteriorly at the level of the fourth cervical vertebra (Figs. 8 to 10). There were severe fractures of the right maxilla and malar-zygomatic compound and also an incomplete fracture of the right condyle of the mandible. Multiple metallic foreign bodies were imbedded in the right cheek and right mastoid region. In addition, there was hemorrhage as well as blast injury of the left leg.

Because of the patient's general condition and the lung injury, local anesthesia was decided upon. The foreign bodies were removed from the neck and mastoid region and a rubber drain was inserted in this area. The right cheek and ear were sutured. The neck

wound was débrided. Eyelet wires were applied to the teeth, and intramaxillary elastic traction was applied for stabilization of the mandibular fracture.

The following day the patient suffered from dyspnea. There was swelling of the aryepiglottic folds. Under local anesthesia, a tracheotomy was performed at which time 500 c.c. of stored blood were administered. He was evacuated on November 4 in good condition.

Fig. 8.

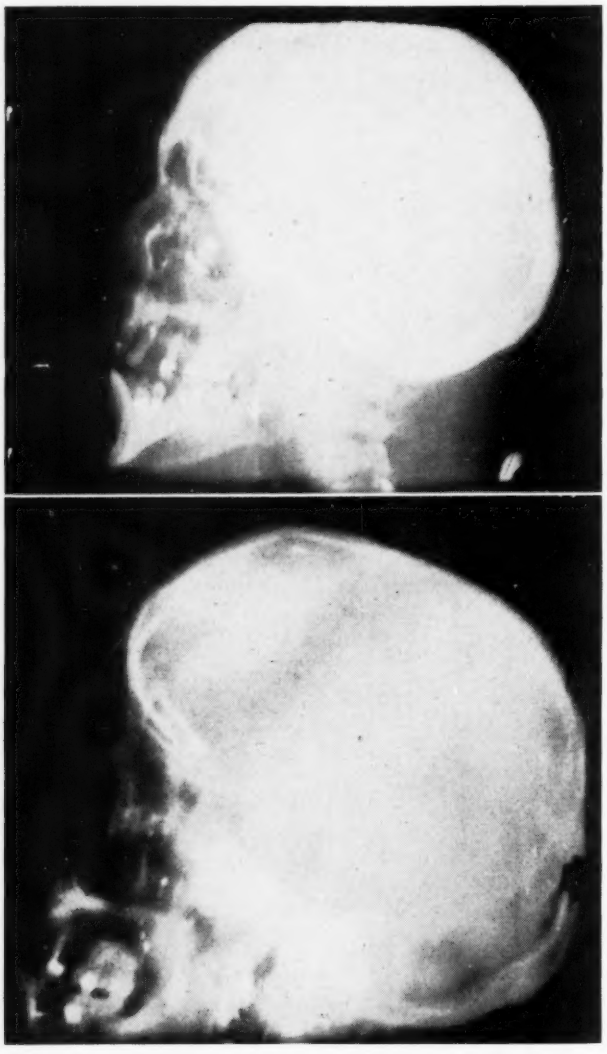


Fig. 9.

Fig. 8 (Case 9).—Lateral x-ray view showing fractures of maxilla and mandible. Several metallic foreign bodies are scattered throughout; note the foreign body posteriorly at the level of the fourth cervical vertebra.

Fig. 9 (Case 9).—Lateral x-ray view. Note the foreign body in the oropharynx, necessitating postoperative tracheotomy, though it was not removed.

CASE 10.—M. A. was admitted to an evacuation hospital in Holland, Oct. 18, 1944. There was a shell wound which had perforated the neck. The point of entrance was below the left angle of the mandible and the missile had coursed along the floor of the mouth.

The exit was below the right angle of the mandible. There was a perforating wound of the pharynx at the level of the epiglottis.

Under endotracheal anesthesia, the pharyngeal perforations were closed by means of exploration from the outside from one mandibular angle to the other across the hyoid bone. Ligature of the right lingual artery was necessary because it bled profusely into the pharynx after it had been severed by the missile.

Tracheotomy was necessary postoperatively because the patient developed dyspnea. It would have been better performed preoperatively. The patient was later evacuated in good condition.

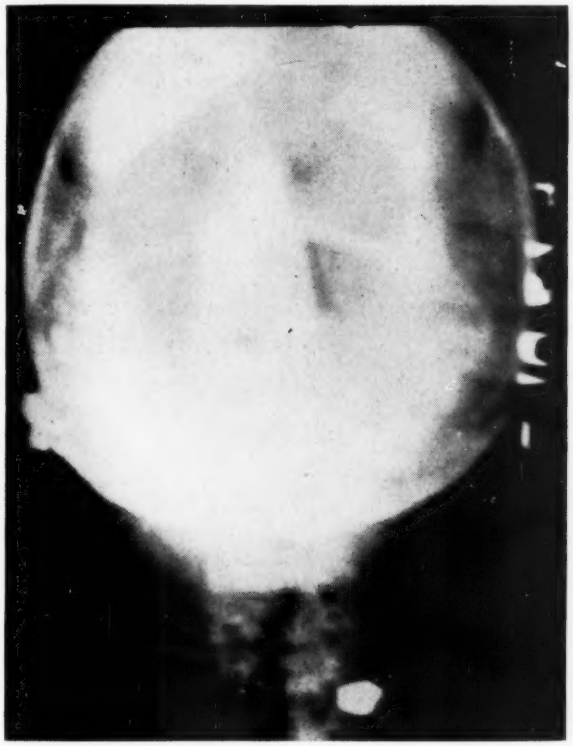


Fig. 10 (Case 9).—Occipitomental view clearly showing fracture of right malar-zygomatic compound; the trachea is seen plainly.

CASE 11.—A patient was admitted to an evacuation hospital in Holland, Jan. 12, 1945. An aerial bomb had caused a perforating wound of the neck (Fig. 11). The wound of entrance was posterior and the wound of exit anterior where there was a large, gaping, lacerated wound in the posterior triangle of the neck.

The wound was débrided, and primary suture of the wound of exit was effected (Fig. 12). A rubber drain was inserted into the wound of entrance. The patient had an uneventful postoperative course and was finally evacuated.

This case is cited as an example of severe neck wound in which tracheotomy was not indicated. The wound was lateral to the great vessels of the neck and did not involve them. The airway was not impinged upon and there was no respiratory obstruction.

Note that in these cases only the salient points were included. Local sulfanilamide or penicillin were used in most cases. Postoperatively, the patients received penicillin and sulfadiazine.

Fig. 11.

Fig. 12.

Fig. 11 (Case 11).—Perforating wound of neck showing large lacerated wound of exit and wound of entrance posteriorly; injury involves the posterior triangle of neck (see Fig. 3).

Fig. 12 (Case 11).—Postoperative view of patient on operating table. Endotracheal anesthesia is being given through a tube in the right nostril. The wound has been closed in layers by primary suture. Note the rubber drain in the wound of entrance.

SUMMARY

1. Tracheotomy is not an operation without hazard and should not be performed unless indicated. When necessary it may be the most important factor in saving the life of the patient.

2. Acute respiratory obstruction when present, and which cannot be relieved by other means, is an obvious indication for tracheotomy. This may occur in (a) penetrating or perforating wounds of the neck because of involvement of the trachea, larynx, pharynx, or the base of the tongue; or (b) secondary involvement of these structures without direct violence, that is, inflammation.

3. Tracheotomy may be indicated in extensive soft tissue injury of the face because of postoperative respiratory obstruction caused by the spread of infection with resultant inflammation and edema of the airway.

4. Tracheotomy may be indicated in extensive involvement of the upper facial bony elements. Postoperative obstruction may be caused by mechanical means or there may be secondary involvement of the pharyngeal structures by the secondary spread of infection.

5. Tracheotomy is sometimes indicated in gunshot wounds of the mandible where there is extensive injury.

6. Proper aftercare as well as care in transit of tracheotomized patients is as important as the operation itself.

7. Case reports typifying these have been presented.

8. Horizontal incision of the skin is the natural and best one for tracheotomy.

REFERENCES

1. Bailey, H.: Surgery of Modern Warfare, chap. 71, Baltimore, 1942, Williams & Wilkins Company, p. 807.
2. Ballenger, W. L., and Ballenger, H. C.: Diseases of Nose, Throat and Ear, chap. 25, New York, 1943, Lea & Febiger, p. 362.
3. Horsley, J. A., and Bigger, I. A.: Operative Surgery, chap. 31, St. Louis, 1937, The C. V. Mosby Company, p. 508.
4. Gray, H.: Anatomy of the Human Body, New York, 1930, Lea & Febiger, p. 1079.
5. Cecil, R. L.: Text-Book of Medicine, Diseases of the Larynx, New York, 1942, W. B. Saunders Company, p. 910.
6. Johnson, W. B., Jr., and Ruzicka, E. R.: Endotracheal Anesthesia for Dental and Oral Surgery, U. S. Nav. M. Bull. **43**: 304, 1944.
7. Junker, I. F.: Med. Times & Hosp. Gaz. **50**: 50, 1872.
8. Macintosh, R. R., and Pratt-Bannister, F. B.: Essentials of General Anaesthesia, Oxford, 1943, Blackwell Scientific Publications, pp. 5-251.
9. Manual of Standard Practice of Plastic and Maxillo-Facial Surgery, vol. II, Philadelphia, 1942, W. B. Saunders Company, p. 269.
10. Thorek, Max: Modern Surgical Technique, vol. I, Philadelphia, 1939, J. B. Lippincott Company, p. 387.

PLEURALIZATION OF THE LEFT BRONCHUS IN PNEUMONECTOMY

ROGELIO BARATA, M.D., HAVANA, CUBA

(From the University Hospital and the Children's Hospital for Tuberculosis)

THE difficulties encountered in my first pneumonectomies regarding the adequate pleuralization of the left bronchial stump, especially in cases of abscesses and bronchiectasis, led me to follow a technique, with such good results, that I believe it should be published.

This procedure always permits the effective pleuralization of the left bronchus whichever the case for the surgical intervention might have been.

It is known that in the left pulmonary pedicle, the anterior pleural flap leaves the mediastinum at the level of the posterior face of the ascending aorta and the posterior pleural flap at the level of the anterior face of descending aorta, there being, between these two segments of the vessel, a distance, variable with the width of the aortic arch, which is always of such a magnitude that when the lung is resected the pleural flaps retire and do not obliterate the mediastinal opening. The efforts to move near the pleural flaps by interrupted sutures produce large lacerations in its surface, leaving the bronchus pleuralized in an incomplete way and, therefore, exposed to the opening.

This difficulty is almost insurmountable in some cases of abscesses where the pleural flaps of the pedicle are inelastic. Experience has taught us that it suffices to apply to the bronchial stump (closed by interrupted sutures of silk or chromic catgut; better results with metallic suture, Surgaloy No. 30) a pleural flap of the pedicle, which should cover it completely to avoid the bronchial fistula, and also that pediculated flaps separated from the posterior parietal pleura are not so effective as the flaps from the pedicle.

TECHNIQUE

Once the pneumonectomy is completed, and after the bronchus is closed (Fig. 1), the mediastinal pleura is separated with the forefinger, following the interior surface of the anterior pleural flap of the pedicle (Fig. 2) to about one inch past the level of the phrenic nerve and the superior diaphragmatic vessels. The phrenic nerve can, at this moment, be crushed above the level where the stitches will be passed.

Following this, various interrupted sutures are made from the posterior face and borders of the bronchus to the ample mediastinal pleural flap which has been made movable. The sutures pass over the phrenic nerve, which, serving as a pulley, will make the pleura descend without lacerations, thus making it possible to apply to the bronchus the pleural flap which will cover it completely (Fig. 3).

Received for publication, June 18, 1946.

When the tying of sutures is being finished, the bronchial stump is displaced to the front, resting against the ascending aorta. If, as occurs in a few cases, a posterior pleural flap can be made use of, everything possible is done to bring about the pleuralization of the total mediastinum, although this is not really necessary to obtain satisfactory results.

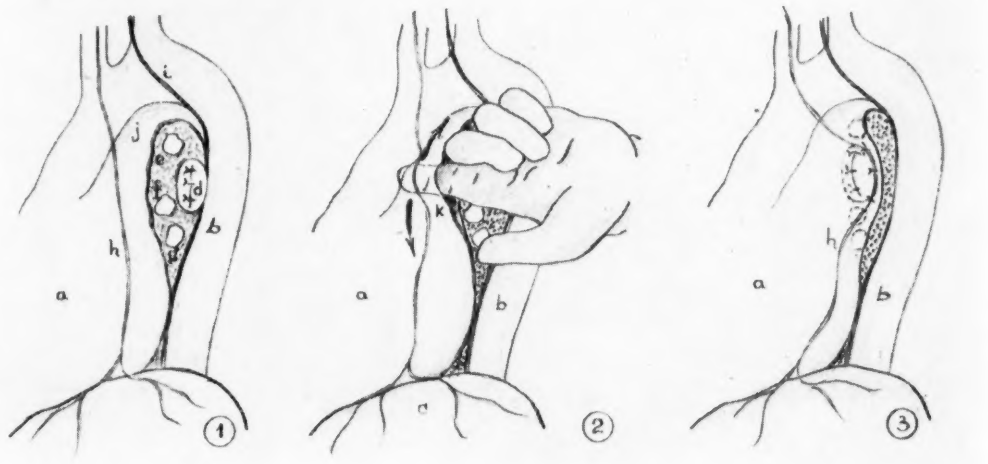


Fig. 1. Fig. 2. Fig. 3.

Fig. 1.—The lung has been resected. (*a*) Heart and pericardium, (*b*) descending aorta, (*e*) pulmonary artery, (*f* and *g*) pulmonary veins, (*h*) phrenic nerve and superior diaphragmatic vessels, and (*i*) neumogastric nerve.

Fig. 2.—Dissection of the anterior pleural flap (*k*).

Fig. 3.—The bronchial stump has been pleuralized by suturing the phrenic nerve and pleura to the posterior face and borders of the bronchus. Note the displacement of the bronchus.

This technique has been successfully used in more than twelve cases. On some occasions, after tying the sutures, the ascending aorta has been slightly compressed, but apparently with no bad effects. This difficulty has been obviated by dissecting a major pleural flap and stretching it, so that it easily reaches the bronchial stump.

REFERENCE

Barata, R.: Estudio anátomo-topográfico del pedículo pulmonar izquierdo y su aplicación a la cirugía pulmonar, Rev. tuberc., Habana 7: 430-434, 1943.

Book Reviews

Penicillin—Its Clinical Application. Under the General Editorship of Professor Sir Alexander Fleming, M.B., B.S., F.R.C.P., F.R.C.S., F.R.S., Professor of Bacteriology in the University of London, St. Mary's Hospital, London. Pp. 380. Illustrated. Philadelphia, 1946, The Blakiston Company. $7.

It is fortunate and fitting that the individual responsible for the discovery of penicillin should edit a definitive monograph on the present status of penicillin for the clinicians. Although other books have been published on this subject, Fleming's effort is the most authoritative and up to date. Recognizing that he was a laboratory worker and not a clinician, Fleming has delegated the presentation of the clinical phases of the subject to various British clinicians. The introductory chapter by Fleming on the "History and Development of Penicillin" is excellent. He gives merited credit to the pioneering efforts of Raistrick and his associates, who endeavored to produce penicillin long before the workers at Oxford. The introductory chapter is followed by informative discussions on the chemistry of penicillin, methods of manufacture, and pharmacology of penicillin. Methods of assaying penicillin are detailed by Fleming in another chapter. Hudson, who is surgeon at Middlesex Hospital, presents a chapter on the treatment of generalized infections. His statement that there is "no definite evidence that organisms can become penicillin-resistant" will not go unchallenged. This does occur, but, fortunately, not too commonly. The management of chest infections is discussed by Gosse of St. Mary's Hospital and chest surgery by Sellars of the London Chest Hospital; the latter is particularly well done. There has been considerable discussion concerning the merits of penicillin in gas gangrene, and the presentation of Porritt and Mitchell indicates a wide and critical experience. They emphasize the major role of surgery in prophylaxis. The advantages of penicillin in osteomyelitis are detailed by Aird of the University of Edinburgh, and this section should be consulted by anyone interested in a good review of the subject. The use of penicillin in sepsis neonatorum is the most comprehensive and well balanced that this reviewer has seen. This also applies to the section on penicillin in brain and meningeal infections written by Wright of St. Mary's Hospital.

Each of the specialties is well represented in this monograph, including dentistry and veterinary medicine. One wonders why such an excellent review of the subject should conclude with a chapter on "Penicillin and the General Practitioner." It is superfluous and not too informative. Clinicians, in general, in the United States will not agree with the enthusiastic recommendations their British colleagues have for the local use of penicillin. Perhaps penicillin was widely utilized in this manner because of the relative scarcity of the drug, but more extensive experience has shown that the topical application of penicillin is too frequently followed by serious reactions of a hypersensitive type.

Sir Alexander Fleming merits congratulations for making this monograph possible. The publishers are to be commended for the make-up of the volume. This work is recommended without hesitation to specialists and to general practitioners.

From every corner of the globe, from every land in which modern surgical methods are known and practiced, come the published reports—now more than 800 in number—on intravenous anesthesia with Pentothal Sodium. This worldwide tribute is gratifying, of course, to the laboratory which developed the drug, but its chief significance is for you. This detailed record provides an invaluable guide covering every phase of the use of Pentothal Sodium—its indications and contraindications, advantages and disadvantages, precautions to be observed, and techniques to be followed. The result is that Pentothal Sodium can be used for intravenous anesthesia with greater safety, more convenience and greater effectiveness. Interested in more facts? Just write to ABBOTT LABORATORIES, North Chicago, Illinois.

Pentothal Sodium

REG. U. S. PAT. OFF.

[Sterile Thiopental Sodium, Abbott]

FOR INTRAVENOUS ANESTHESIA

New Pentothal Film

Medical groups interested in intravenous anesthesia may arrange for the showing of a new motion picture film on the use of Pentothal Sodium by writing to the Medical Department, ABBOTT LABORATORIES, North Chicago, Illinois.

People everywhere respect the symbol of the Red Cross—
Because it knows no boundaries of race, color or creed
Because its sole concern is for the good of mankind
Because it serves our men in the armed forces—helps veterans—is ever present when disaster strikes.
The warm heart of America expresses itself through the Red Cross . . . Give generously to the 1947 Fund.

BASIL O'CONNOR, Chairman
The American National Red Cross

JUST ISSUED

BONE AND BONES

Fundamentals of Bone Biology

THE authors have written this volume in an effort to summarize and unify, and at the same time offer a detached survey of facts and theories which diminishes details but permits a vision of the greater plan.

In the preface, they state, "The book is intended to be a challenge to the research worker; a guide to those who work on bone and on bones in their medical specialty: orthopedists, radiologists, metabolists, dentists, orthodontists; and an aid to the teacher who wants to integrate his particular field into the greater unit of biology."

A PATHOLOGIST AND AN ANATOMIST *each with a working knowledge of the other's field* HAVE JOINED FORCES TO CREATE THIS NEW AND UNUSUALLY VALUABLE WORK—

By JOSEPH P. WEINMANN, M.D., and HARRY SICHER, M.D. Department of Research, School of Dentistry, Loyola University, Chicago College of Dental Surgery

464 pages, with 289 illustrations. Price, cloth, $10.00.

The C. V. Mosby Company—Medical Publishers—St. Louis, U. S. A.

"Of inestimable value as a ready reference guide . . ."
—*West. Jnl. S. O. & G.*

". . . this unique volume marks an important milestone in surgical advance . . ."
—*Jnl. Bone & Joint Surgery*

Bunnell Surgery of The Hand

"The scope of Dr. Bunnell's book is truly amazing . . ."
—*Southern Medical Jnl.*

"Bunnell's masterpiece should be a standard reference text. . . ."
—*U. S. Naval Medical Bulletin*

BY STERLING BUNNELL, M.D., *Honorary Member of American Academy of Orthopedic Surgeons; Member of American Association of Plastic Surgeons and of American Society of Plastic and Reconstructive Surgery; Licentiate of American Board of General Surgery and Plastic Surgery.*

Dr. Bunnell's important book tells the practitioner and surgeon how to successfully restore function in injuries of the hand.

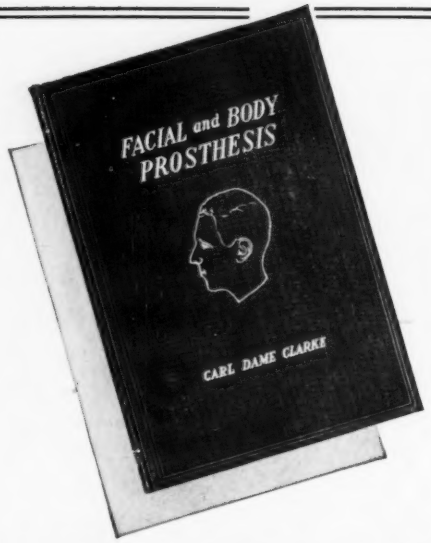
Surgery of The Hand discusses the normal hand with phylogeny and comparative anatomy; the basic principles of examination and technics of reconstruction; injuries and infections of the hand; deformities, vasomotor and trophic conditions, and tumors of the hand. The excellent illustrations were all supervised by Dr. Bunnell and many were actually drawn by him.

734 pages
597 Illustrations
2 Color Plates
$12.00

J. B. LIPPINCOTT COMPANY, East Washington Square, Phila. 5, Pa. S547
Enter my order and send me:
Bunnell—SURGERY OF THE HAND—$12.00
( ) Cash Enclosed ( ) Charge my account ( ) Send C.O.D.
Name_____
Street_____
City, Zone, State_____
Under your guarantee, I may return book within ten days, otherwise I will pay in full within 30 days.

A LIPPINCOTT SELECTED PROFESSIONAL BOOK
DROIT ET AVANT

LIPPINCOTT SELECTED PROFESSIONAL BOOKS



Clarke's FACIAL and BODY PROSTHESIS

by **CARL DAME CLARKE,** Associate Professor of Art as Applied to Medicine, School of Medicine, University of Maryland; Captain, Sanitary Corps Army of the United States, Department of Moulage and Prosthetics, Army Medical Museum.

200 pages, 75 illustrations. $5.00

THE C. V. MOSBY COMPANY
3207 Washington Blvd.
St. Louis 3, Mo.

"Facial and Body Prosthesis" emphasizes the importance of prosthesis as a method of repair high in cosmetic, psychologic and physical value. Its text and illustrations demonstrate this vividly, and at the same time instruct in every aspect, every stage of repair by this means. Whether you require this knowledge for actual practice—or for advisory purposes, you will find "Facial and Body Prosthesis" a valuable tool. Let us send your copy now.

Back Copies WANTED!

The publishers require copies of the following back issues of Surgery, mostly for libraries, to complete broken files:

November,	**1942**
October, December	**1943**
January, November	**1944**
January,	**1946**

We will pay $0.85 for each copy

Address copies to: *A. W. Volland,* Circulation Manager The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Missouri.

Only 385 Copies Remain in Print

1938 TRANSACTIONS
OF THE
THIRD INTERNATIONAL GOITER CONFERENCE
AND THE
AMERICAN ASSOCIATION
FOR THE **STUDY OF GOITER**

Available to the Profession at only $4.50 per copy
A 25% reduction from original cost

"THE *vade mecum* of the thyroid gland problem." Comprehensive, authoritative documentation on goiter for the decade following the 1927 International Goiter Conference in Berne, Switzerland • Sixty preeminent contributors, each a recognized leader in the specialty in the United States, Canada, Europe or South America, including Lang, Welti, Eggenberger, Wegelin, Collip, Loeser, Wahlberg, Puppel, Rienhoff, Pemberton, Thompson, Crile, Crotto, Rawson, Marine, Haines, Cattell, Means, Lahey, and Bartels • 545 pages, profusely illustrated bound in gold-stamped fabrikoid. To be sold at only $4.50, including postage; a 25 per cent reduction from the original cost.

ORDER NOW to insure your possession of one or more of the 385 copies of this essential volume remaining in print

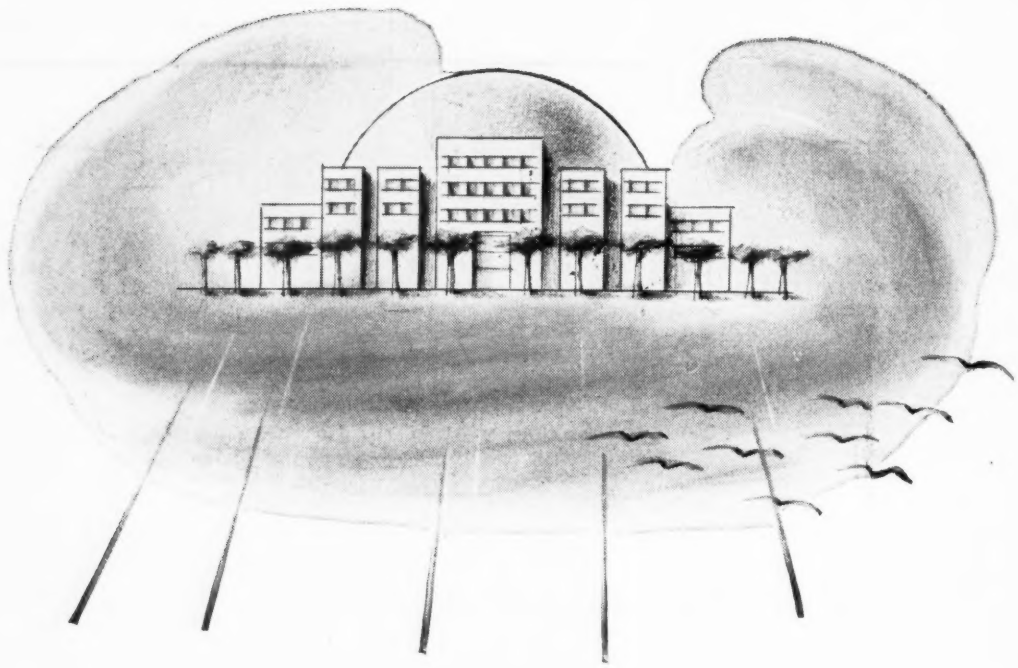
WESTERN JOURNAL of SURGERY PUBLISHING CO.
302 PHOENIX BLDG., PORTLAND 4, ORE.

Fill in and mail this Order Form Today!

Gentlemen:
Please enter my order for_____copies of 1938 Transactions of the Third International Goiter Conference and the American Association for the Study of Goiter, at $4.50 per copy postpaid.
Check enclosed_____. Bill me_____

_____M.D.

Address_____ City_____ State_____



Dream Hospital . . .

The hospital depicted here exists only in the hearts of men and women who are losing the grim battle with cancer. And in the imagination of other men and women who want desperately to provide a haven for these victims in need of hope and care to sustain them in the few months or years still remaining to them.

Actually, there is not a single such hospital anywhere devoted exclusively to these unfortunates who *may* be beyond the help of medical sciences, but who are still certainly in urgent need of hospital care. And only a limited, woefully insufficient number of beds available to them in other hospitals.

During the long years of the war we gave up our plans for the building of this dream hospital . . . **Hope Institute.**

But now we are more than ever determined to see it rise in stone and steel. A model hospital, the first of its kind . . . cheerful and comfortable in every way . . . with more the atmosphere of an apartment hotel than of a cold institution. Where the patients, depending upon their condition, can enjoy the warm hospitality of lounge and dining room, or retire to the merciful seclusion of a private room.

What do we need to build this hospital now? **You.** Every dollar or penny you can scrape together for it. Whether or not you know this tragedy from bitter personal experience . . . the tragedy of whole families, endlessly frustrated in their determination to care for a doomed member . . . give as generously as you can. Please fill out the coupon below and mail with your contribution. It will make this hospital more than a dream.

NCF

THE NATIONAL CANCER FOUNDATION
Griffin Building, 85 Franklin Street, New York 13, N. Y.

NAME _____

ADDRESS _____

Make checks payable to Abbott Kimball, Treasurer of the National Cancer Foundation.

THE NATIONAL CANCER FOUNDATION

Affiliated with

SPONSORS OF GOVERNMENT ACTION AGAINST CANCER

THE NATIONAL FOUNDATION FOR THE CARE OF ADVANCED CANCER PATIENTS

Books and World Recovery

THE desperate and continued need for American publications to serve as tools of physical and intellectual reconstruction abroad has been made vividly apparent by appeals from scholars in many lands. The American Book Center for War Devastated Libraries has been urged to continue meeting this need at least through 1947. The Book Center is therefore making a renewed appeal for American books and periodicals—for *technical and scholarly books and periodicals in all fields* and particularly for *publications of the past ten years.* We shall especially welcome complete or incomplete files of publications of the C. V. Mosby Company.

The generous support which has been given to the Book Center has made it possible to ship more than 700,000 volumes abroad in the past year. It is hoped to double this amount before the Book Center closes. The books and periodicals which your personal or institutional library can spare are urgently needed and will help in the reconstruction which must preface world understanding and peace.

Ship your contributions to the *American Book Center, c/o The Library of Congress, Washington 25, D. C.,* freight prepaid, or write to the Center for further information.

Just Issued!

Rubin's UTEROTUBAL INSUFFLATION

by

I. C. RUBIN, M.D., F.A.C.S., Clinical Professor of Gynecology, College of Physicians and Surgeons, Columbia University, New York.

453 pages, 159 illustrations, including 6 in color. Price, cloth, $10.00

A Clinical Diagnostic Method of Determining the Tubal Factor in Sterility Including Therapeutic Aspects & Comparative Notes on Hysterosalpingography

- **Clinical Viewpoint Stressed and Maintained . . .**
- **Data Gathered over 25-Year Period . . .**
- **Much Hitherto Unpublished Material Presented . . .**

THE C. V. MOSBY COMPANY

3207 Washington Blvd. St. Louis 3, Mo.

SURGERY

Editors: ALTON OCHSNER, M.D., 1430 Tulane Ave., New Orleans, La., and OWEN H. WANGENSTEEN, M.D., University Hospitals, Minneapolis, Minn.

Associate Editor: ALFRED BLALOCK, M.D., Johns Hopkins Hospital, Baltimore, Md.

Published by THE C. V. MOSBY COMPANY, 3207 Washington Blvd., St. Louis 3, U.S.A.

Great Britain Agents: Henry Kimpton, Ltd., 26 Bloomsbury Way, London, W.C.1.
Entered at the Post Office at St. Louis, Mo., as Second-Class Matter.

Published Monthly. Subscriptions may begin at any time.

Editorial Communications

Original Communications.—This Journal invites concise original articles of new matter in the broad field of clinical and experimental surgery. Descriptions of new techniques and methods are welcomed. Articles are accepted for publication with the understanding that they are contributed solely to SURGERY.

Manuscripts submitted for publication may be sent to Dr. Alton Ochsner, 1430 Tulane Avenue, New Orleans, Louisiana, or to Dr. Owen H. Wangensteen, University Hospitals, Minneapolis, Minnesota.

Neither the editors nor the publishers accept responsibility for the views and statements of authors expressed in their communications.

Translations.—Manuscripts written in a foreign language, if found suitable for publication, will be translated without cost to the author.

Manuscripts.—Manuscripts should be typewritten on one side of the paper only, with double spacing and liberal margins. References should be placed at the end of the article and should conform to the style of the Quarterly Cumulative Index Medicus; viz., name of author, title of article, and name of periodical with volume, page, and year. Illustrations accompanying manuscripts should be numbered, provided with suitable legends, and marked on margin or back with the author's name.

Authors should indicate on the manuscript the approximate position of text figures. The original drawings, not photographs of them, should accompany the manuscript.

Illustrations.—A reasonable number of half-tone illustrations will be reproduced free of cost to the author, but special arrangements must be made with the editors for color plates, elaborate tables or extra illustrations. Copy for zinc cuts (such as pen drawings and charts) should be drawn and lettered only in India ink, or black typewriter ribbon (when the typewriter is used), as ordinary blue ink or colors will not reproduce. Only good photographic prints or drawings should be supplied for half-tone work.

Exchanges.—Contributions, letters, exchanges, reprints, and all other communications relating to SURGERY should be sent to one of the editors.

Review of Books.—Books and monographs, native and foreign, will be reviewed according to their merits and as space permits. Books may be sent to Dr. Owen H. Wangensteen, University Hospitals, Minneapolis, Minn.

Reprints.—Reprints of articles published among "Original Communications" must be ordered directly through the publishers, The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, U.S.A., who will send their schedule of prices. Individual reprints of an article must be obtained through the author.

Business Communications

Business Communications.—All communications in regard to advertising, subscriptions, change of address, etc., should be addressed to the publishers, The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo.

Subscription Rates.—Single copies, 85 cents. In the United States and its Possessions and the Pan-American Countries, $10.00 per year in advance. Canada and other Foreign Countries, $11.00. Includes two volumes a year, January and July.

Remittances.—Remittances for subscriptions should be made by check, draft, post office or express money order, or registered letter, payable to the publishers, The C. V. Mosby Co.

Change of Address.—The publishers should be advised of change of subscriber's address about fifteen days before the date of issue, with both new and old addresses given.

Advertisements.—Only articles of known scientific value will be given space. Forms close tenth of month preceding date of issue. Advertising rates and page sizes on application.

This car is running with an "EMPTY" gas tank!

EVEN AFTER the gas gauge says "empty" a modern car can keep going for a good many miles. Here's why.

Automobile manufacturers know human nature. They figure that, sooner or later, we'll get careless, or misjudge how far we have to go. So the gas gauge is set to show "empty," while there are still a couple of gallons left in the tank.

This reserve supply is a swell idea that has kept many a family from getting stuck.

It's an even better idea for a family's budget!

A reserve supply of dollars is a lifesaver in case of financial emergency. It will keep your family going if sudden illness strikes, or unexpected expenses show up.

And one of the easiest ways to build just such a cash reserve is *buying U. S. Savings Bonds on the Payroll Savings Plan!*

Millions of Americans have discovered that *automatic* Bond buying is the quickest, surest way of saving money. What's more, the money you save in Bonds buckles right down and starts *making more money*—in just 10 years you get back $100 for every $75 you put in today.

So keep on buying Bonds on the Payroll Plan. Buy all the extra Bonds you can, at any bank or post office. And remember, you're helping your country as well as yourself—for every Bond you buy plays a part in keeping the U. S. strong and economically sound!

Save the easy way..buy your bonds through payroll savings

Contributed by this magazine in co-operation with the Magazine Publishers of America as a public service.

A PUBLIC SERVICE PROJECT — The Advertising Council

INDEX TO ADVERTISERS

Please mention "SURGERY" when writing to our advertisers—It identifies you

Abbott Laboratories (Pentothal Sodium) ---- 15
American Book Center ---- 21
American Red Cross ---- 16
Articles to Appear in Early Issues ---- Third Cover

Back Copies Wanted ---- 12

Ciba Pharmaceutical Products, Inc. (Di-Ovocylin) ---- 5

Davis & Geck, Inc. (Sutures) ---- 3

Ethicon Suture Laboratories (Sutures) 13

Gomco Surgical Manufacturing Corp. (Tidal Irrigator) ---- 12
Gudebrod Brothers Silk Co., Inc. (Sutures) ---- 4

Hoffmann-La Roche, Inc. (Prostigmin) ---- Fourth Cover

Lilly and Company, Eli (Pulvules Tuinal) ---- 14
Lippincott Company, J. B. (Books) ---- 17

National Cancer Foundation, The ---- 20

Pilling & Son Company, George P. (Surgical Instruments) ---- 1

Schering Corporation (Oreton) ---- 9
Singer Sewing Machine Company (Surgical Stitching Instrument) ---- 2
Stearns & Company, Frederick (Mucilose) ---- 11
Suckert Loose Leaf Co. (Journal Binder) ---- 12

U. S. Savings Bonds ---- 23

Veterans of Foreign Wars of the United States (Poppy Sale) ---- 18

Western Journal of Surgery Publishing Company (Transactions of the Society for the Study of Goiter) ---- 19
White Laboratories, Inc. (Mol-Iron) 6, 7
Wyeth Incorporated (Petrogalar) ---- 8

All possible care is exercised in the preparation of this index. The publishers are not responsible for any errors or omissions.

Key and Conwell's

4th Revised Edition

FRACTURES, DISLOCATIONS AND SPRAINS

- More than 200 new illustrations added and substituted.
- All recent developments in theory and practice included.
- Section on war wounds revised especially with regard to skeletal fixation and chemotherapy.
- Complete revision of the chapter on Injuries of the Spine. Davis contributes a description of his gravity suspension method for the treatment of compression fractures of the spine and the section on cervical fractures and dislocations.

By John Albert Key, B.S., M.D., and H. Earle Conwell, M.D., F.A.C.S.

1300 pages Price, $15.00 1316 illustrations

THE C. V. MOSBY COMPANY — Publishers — ST. LOUIS 3, MO